SCIENCE

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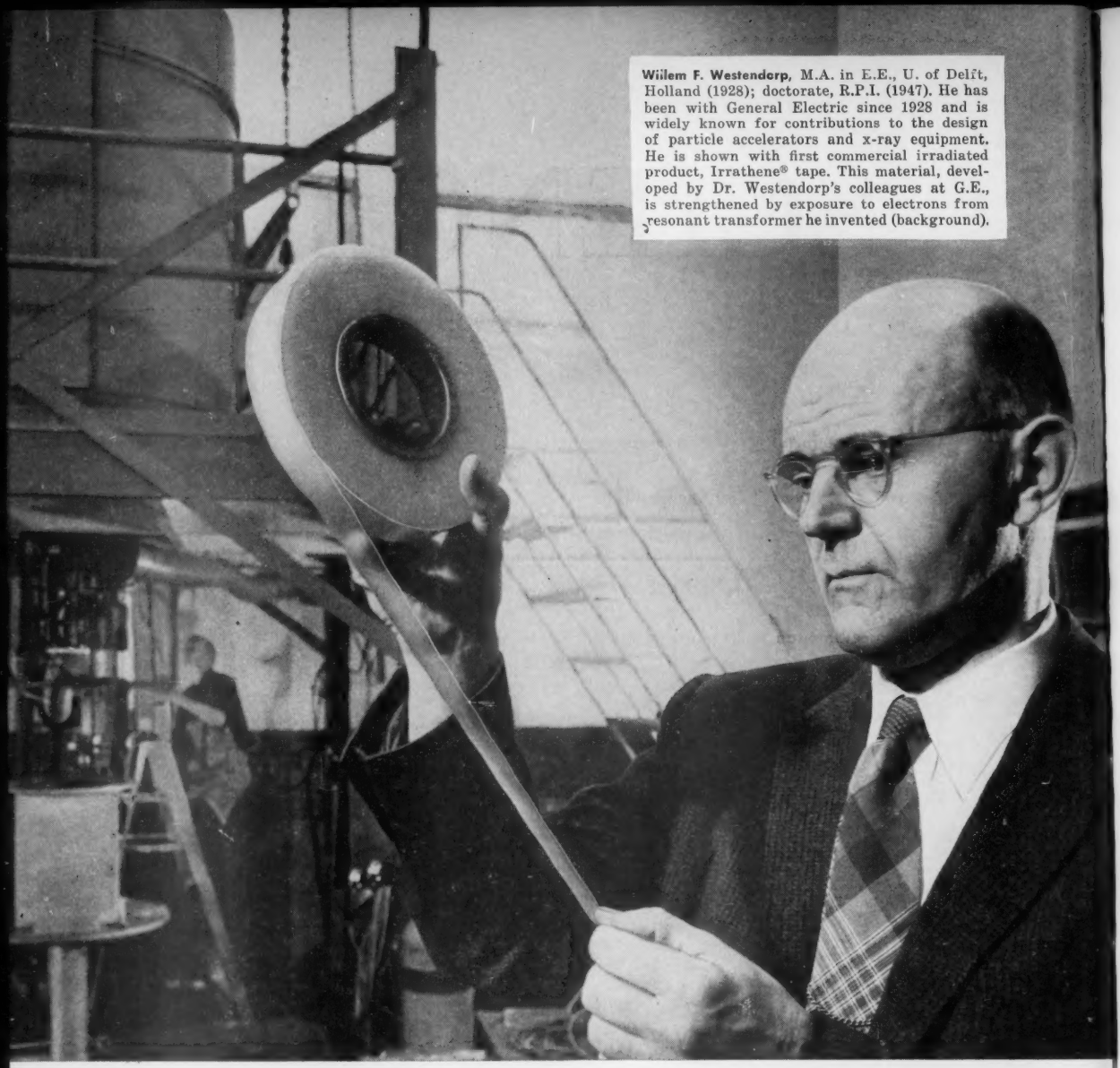

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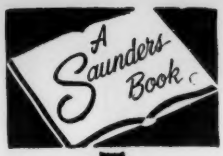

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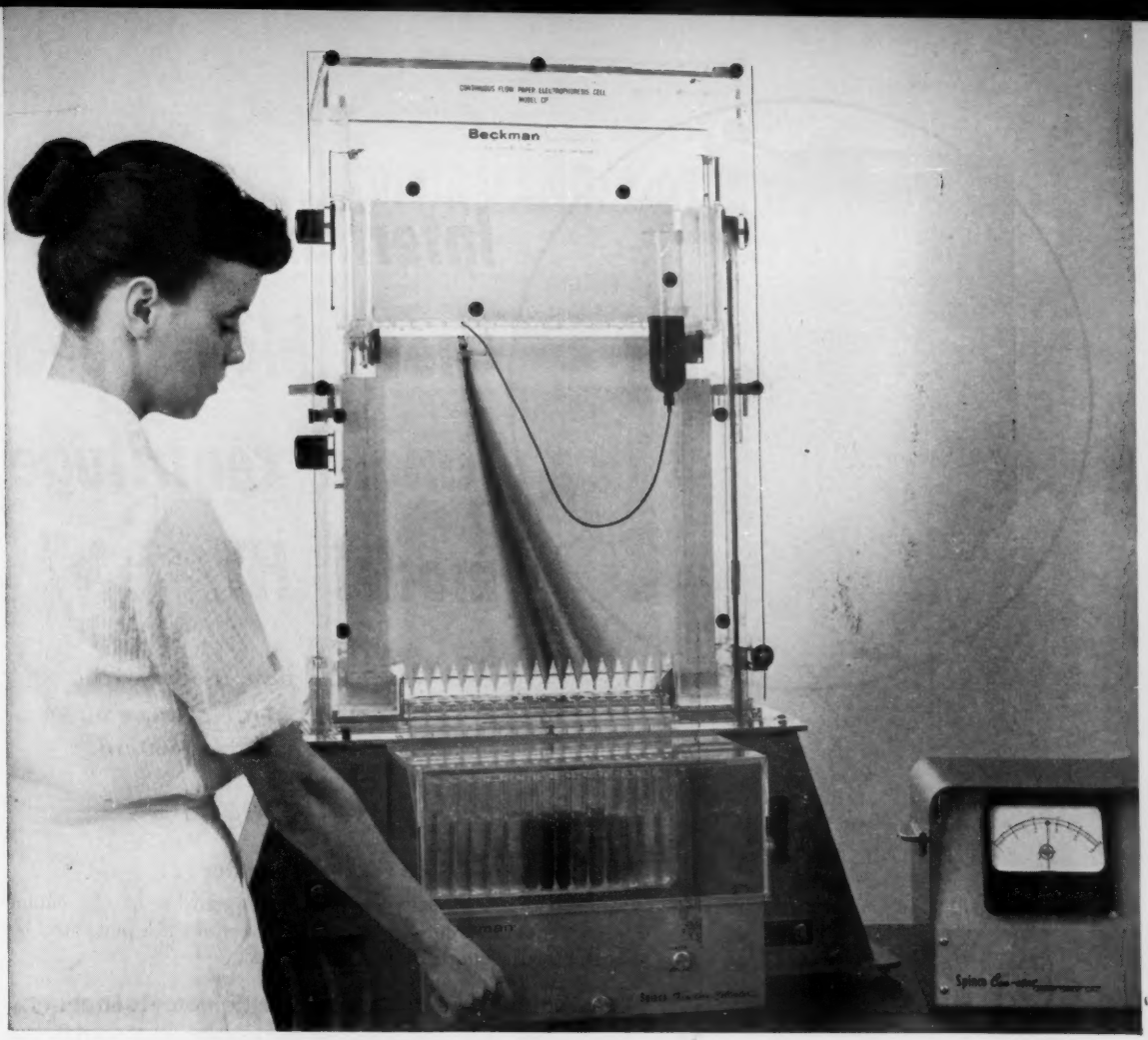

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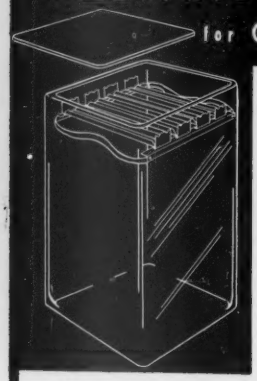

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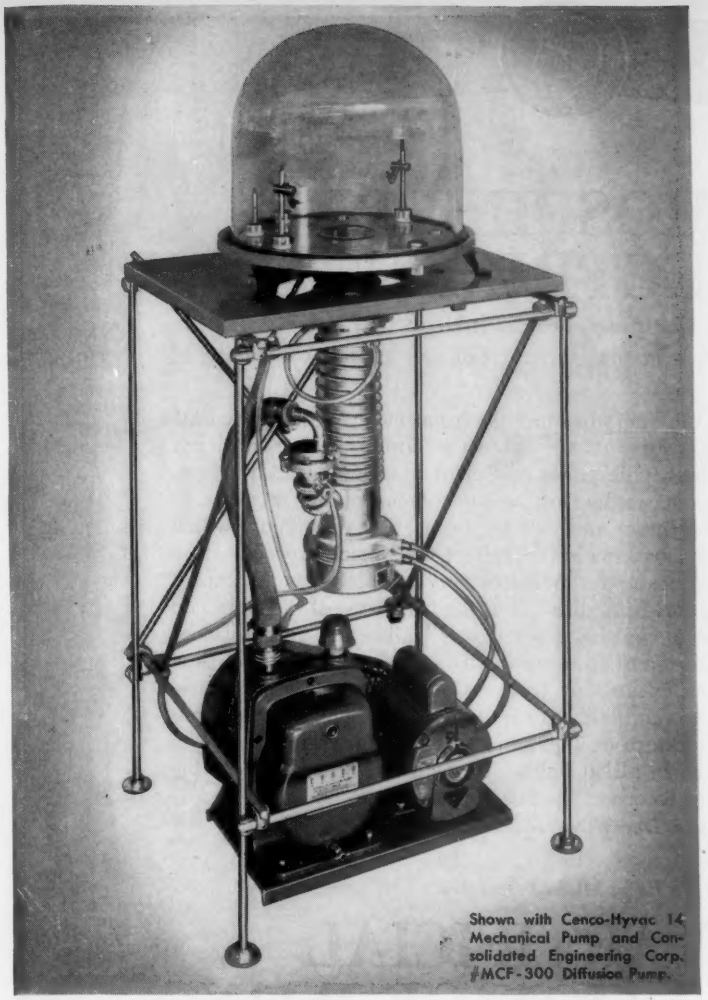

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The AAAS also publishes THE SCIENTIFIC MONTHLY.

AAAS Dues Increase

At the meeting of the AAAS Council last December it was proposed from the floor that the association should consider raising its dues—a step which most other associations and scientific societies have found necessary within the past 10 years. This proposal was considered in detail by the AAAS Board of Directors at its March meeting.

Although there has been a gratifying increase in AAAS membership, which now stands at an all-time high of approximately 53,000, there was a small deficit at the close of the association's books for 1956. In the past few years, despite economies and continued efficient practices, the margin between income and outgo has been progressively narrower. Under these circumstances, the board concluded that the time had come for an increase in the annual dues of the association. Accordingly, the board voted unanimously to submit to the council a recommendation that the dues be increased from $6.50 to $8.50 per year, effective 1 January 1958. This recommendation met with approval by 87 percent of the large majority of the council members who returned the mail ballot.

The dues of the association were last changed, from $5 to $6.50, on 1 January 1948. They were changed then for the same reasons as now—a continued increase in such operating expenses as salaries and especially the printing costs of the association's journals and other publications. Then, as now, there was a reluctance on the part of the board and the council to curtail any AAAS activities which had proved their worth or to reduce the quality of the publications. As before, increases in membership and in advertising revenue have made it possible to postpone but not to avoid an increase in dues.

The AAAS has been fortunate in being able to charge smaller dues than most other associations. Two recent studies, one by the National Education Association and the other by the American Marketing Association, have shown that the median annual dues for professional associations are $10, which is also the median for associations with 20,000 or more members. AAAS dues have been in the low category for scientific and professional associations and can well remain below the median figure of $10 for the foreseeable future.

No one has to be told that the costs of goods have increased markedly in the last decade and that often the increase has occurred without a corresponding increase in the intrinsic value of the products. It is fortunate that the AAAS does not have to follow this pattern. The dues increase will be enough to pay the increased costs of an enlarged weekly journal, the combined *Science* and *The Scientific Monthly*, as approved by the council last December. Thus, beginning next January, all members who now receive one of the journals will receive the enlarged weekly *Science*, and those who now receive both journals for $10 per year will get about the same amount of material for $8.50.

An equitable plan for putting the increase into effect has been developed. Present members whose terms expire on or before 1 October 1957 may renew their membership for an entire year at the current rate of $6.50. Similarly, new members who join on or before that date will be accepted at the same rate. Members whose terms begin at subsequent dates will be billed at the new rate of $8.50.

It is hoped that the combination of the two journals and the association's increased soope of activities will meet with approval by all present members and that a continued growth in association membership will occur during its 110th year. The AAAS has grown in its services to science and society and is needed today more than ever.

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First Steps toward a Genetic Chemistry

Robert L. Sinsheimer

The development of a genetic chemistry—a chemistry of the genetic substance—will undoubtedly be a long and exacting and inspiring task. As genetics is a central theme in the science of biology, so we may expect genetic chemistry to become, in time, an integrating core for cellular biochemistry.

The goals of a genetic chemistry, to the extent that we are presently able to define such goals, will be to achieve an understanding of the physical nature of the hereditary units and of the variations these units undergo during the various phases of the life of the cell, to learn how these units are reproduced from generation to generation, to learn how they are modified by extrinsic or intrinsic factors, and to learn in precise chemical terms how they influence the manifold activities of the cells in which they reside.

We are most certainly a long way from these goals, and the paths to their achievement are by no means obvious. Yet I should like to summarize the evidence which leads us to believe, with near certainty, that we have taken a first and essential step toward the creation of a genetic chemistry—that we have, at least, identified one of the principal constituents of the gene. As we review this evidence, I believe it will be possible at the same time to provide a comprehensive summary of the current status of genetic chemistry and of the at least more immediate prospects for further advance.

The author is professor of biophysics at Iowa State College of Agriculture and Mechanic Arts, Ames. This article is based on a lecture presented at California Institute of Technology on 16 Nov. 1956.

When I was preparing this article, I thought back to what was said about my subject—that is, about the physical nature of the gene—in the course in elementary genetics which I had some years ago. To the best that I could recall, nothing was said about it. I attributed this curious result to the passage of years and to an overcrowded memory, so I thought it might be of interest to see how this subject is treated in a current textbook. I examined the book which is presently in use in the basic genetics course at Iowa State College, and after a fairly assiduous search I managed to find one hint that the gene is composed of something more substantial than ectoplasm. In the introductory chapter the statement appeared, "We shall discover that hereditary factors are complex protein molecules which we call genes." Fortunately this thesis was not developed further in the text.

As many know, there is a small but vociferous group who would like to modify that quotation and replace the word *protein* by the term *nucleic acid*—in particular, by *deoxyribose nucleic acid*, or DNA. Now so much has been written and uttered and speculated about DNA in the past few years that I am sure the concept that DNA has something to do with genetics is hardly new to you. What I shall do is to attempt to summarize, a bit critically, the evidence which has been accumulated, very largely within the past decade, that links DNA with the hereditary factors—that is, the genes. In so doing, I should like particularly to distinguish that which we believe we know, and that which, in truth, we merely suspect.

The evidence which links the chemistry of the gene with the chemistry of DNA is at present necessarily circumstantial. Such must be the case until we become sufficiently advanced in our understanding that we are able to demonstrate the action of a gene *in vitro*. But circumstantial evidence can be of varied degrees of credibility. The value of circumstantial evidence is, roughly, inversely proportional to the number of alternative explanations that one can advance for the observed phenomenon. The following eight lines of evidence, which are listed in a rough order of increasing significance, are, I believe, important in establishing a correlation that links DNA and the hereditary factors: (i) the location of DNA; (ii) the specific diploid content of DNA; (iii) the metabolic stability of DNA; (iv) the complementary structure of DNA; (v) the similarity of the ultraviolet absorption spectrum of DNA and the ultraviolet action spectra for mutation; (vi) the nature of the transforming factor; (vii) the role of DNA in bacterial virus infection; (viii) the parallel transfer of genes and DNA in bacterial mating.

The first five of these lines of evidence are the more indirect, and, essentially, they serve merely to present DNA as a likely candidate for a genetic role. The last three are more explicit. In essence they tell us that, in those instances where we observe hereditary factors to enter a cell, the substance DNA enters in a parallel manner—and, indeed, in two instances, only DNA is observed to enter. I should now like to discuss these links in somewhat more detail.

Location

The earliest circumstantial evidence for our thesis was simply that of location. One finds DNA in the structures where one might expect to find genes—50 to 60 percent of the dry mass of a sperm head is DNA (*1*). Within cells, DNA, with a few rare exceptions, is confined to the chromosomes, and within the chromosomes it is localized to bands (*2*), the same bands to which genetic analysis had earlier assigned the hereditary factors.

The principal value of this line of evidence, which is qualitative and indirect, was heuristic. It suggested that it just

Table 1. DNA complement (haploid) of various organisms.

Organism	DNA complement (g)
T2 Bacteriophage	0.0002×10^{-12} per particle
Escherichia coli	0.01×10^{-12} per cell
Sponge	0.06×10^{-12} per cell
Coelenterate	0.3×10^{-12} per cell
Echinoderm	0.9×10^{-12} per cell
Teleosts	$0.5–1.5 \times 10^{-12}$ per cell
Birds	$1–2.0 \times 10^{-12}$ per cell
Turtle	2.5×10^{-12} per cell
Man	2.9×10^{-12} per cell
Rat	3.0×10^{-12} per cell
Cow	3.2×10^{-12} per cell
Frog	7.5×10^{-12} per cell
Dipnoi	50×10^{-12} per cell
Amphiuma	84×10^{-12} per cell
Lillium	53×10^{-12} per cell

might be worth while to know a great deal more about DNA. And historically this evidence played a large role in the rescue of the nucleic acids from some 70 years of neglect.

Specific Diploid Content

It was a logical extension of this morphological implication to inquire whether DNA could satisfy the quantitative requirements of a specifically genetic substance. On morphological grounds, it is believed that all cells of an adult organism have a full diploid complement of chromosomes, with the exception, of course, of the gametes, which have a haploid complement. And careful measurements (*3*) have shown that, if appropriate corrections for polyploidy are made, the DNA content per cell is uniform among all the various types of tissues with the exception of the gametes, which have one-half the normal amount. Again, in polyploid cells the DNA content appears to be discretely 2 or 4 or 8 times the diploid value (*4*). Thus for a particular species, the DNA content accurately parallels the chromosome complement. Indeed, the constancy of DNA content has provided the biochemist with an excellent reference point to use in comparisons of the compositions of various tissues (*5*).

Another type of quantitative correlation that was attempted in this manner did not prove quite so successful. It might have been pleasing if one could have correlated the diploid DNA content with biological complexity. One might have expected that, in the course of evolution, the development of more complex organisms was associated with a greater and more varied DNA content. To some extent this is true, but as Table 1 indicates, the exceptions are such as to make the whole hypothesis at present rather suspect (*6*).

While the constancy of the diploid content of DNA was a pleasing confirmation of our hypothesis, this result raised certain questions. This constancy obviously could not be true of a growing tissue. The DNA content of the cell must double at some stage. This thought has led to several experiments which indicate that the duration of DNA synthesis is relatively brief and that synthesis generally occurs in interphase or in early prophase (*7*). Furthermore, the constancy of over-all DNA content raises anew the question of the physical basis of cellular differentiation. Many people of course believe differentiation to be a matter of cytoplasmic origin rather than of nuclear basis. Frankly, this view affronts my sense of cellular integration. The constancy of DNA content does seem to imply that differentiation is not a matter of the loss of certain genes or of excess replication of others. But it does not indicate that all the genes are functional. And, indeed, there are several lines of evidence which suggest that not all the DNA of mature cells is in the same physical state. Studies by enzymic extraction of nuclei (*8*), by salt extraction of tissue (*9*), by fractionation of isolated DNA (*10*), and studies of methyl-green binding in nuclei (*11*) suggest that the associations between DNA and other cellular constituents are not uniform within a cell and are physiologically variable. I would suggest that investigation of these leads with more refined techniques could prove to be of great value.

Metabolic Stability

The third item of indirect evidence associating DNA with the gene is the matter of the metabolic stability of DNA. This is certainly not a sufficient proof, nor is it really even necessary, but in a way it is satisfying to believe that the physical basis of the gene—the factor that is passed on from cell generation to cell generation—is physically conserved in the process. Despite several apparently misleading reports, it now appears to be generally agreed that DNA is metabolically inert—once an atom is incorporated into a DNA molecule, it remains there for the life of the cell (*12*). The only evidence with which I am familiar which appears contrary to this conclusion is that of Zamenhof on the incorporation of bromouracil into DNA in bacteria in stationary phase (*13*). This may be a special situation.

The metabolic stability of DNA in turn permits one to exclude certain hypotheses concerning its function. However DNA may function, it is clearly not, for instance, a precursor of cytoplasmic ribose nucleic acid (RNA), nor does it seem to form linkages with other substances that would labilize its components. These are negative conclusions, but they help to delimit the problem.

Structure

As we continue our list of associations and properties which suggest that DNA is a highly logical candidate for the gene, we might observe that the very structure of DNA is at least compatible with this notion. Indeed, Hershey (*14*) has said, "If one wished to invent a genetic material, one would almost certainly choose a DNA constituted along the lines proposed by Watson and Crick."

The generally accepted structure for DNA is the two-ply helix first proposed by Watson and Crick (*15*) and shown in Fig. 1. Each chain is a string of nucleotides, of which there are four or five kinds in a given chain. The nucleotides each contain a phosphate residue, a deoxyribose, and one of the purine or pyrimidine bases shown in Figs. 2 and 3. The two chains of the helix are complementary in that specification of one enables one, almost, to specify the other. Ade-

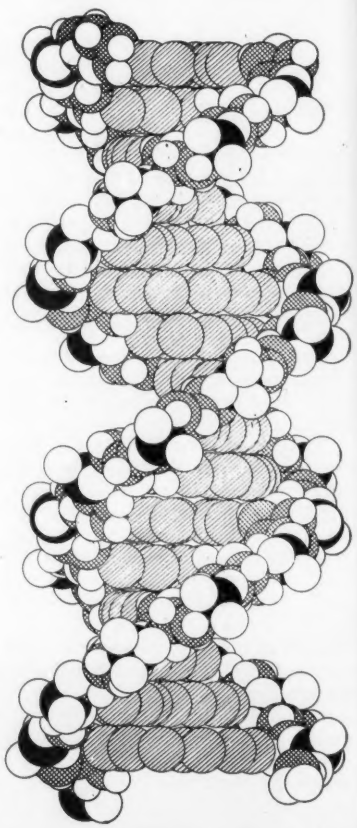

Fig. 1. Molecular model of the two-strand helix of DNA. [Courtesy of L. D. Hamilton]

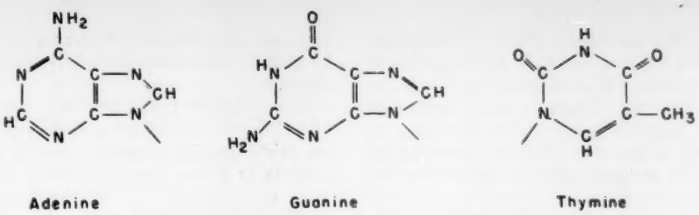

Fig. 2. Three heterocyclic groups found in all DNA preparations.

nine is always opposite thymine and guanine is opposite cytosine (Fig. 4). Then the basic information, which if it is a gene, DNA must carry, is postulated to reside in the sequence of nucleotides along the chain. This information is thus present twice—a nice bit of insurance against the disaster which would ensue upon the loss of a gene. I might interject that there is no experimental evidence at all to support this postulate that the information is carried as a nucleotide sequence—we simply lack any credible alternative hypothesis.

As a further bit of fancy, it has been suggested that when the DNA is to be duplicated, the chains in some manner separate, perhaps only a small segment at a time, and each chain serves as a template upon which to build up its complement, resulting in two chains like the original. Various modes of accomplishing this feat have been proposed which would result in various distributions of the original parental material among the daughters (*16*).

I would like to comment briefly on the Watson-Crick structure and the associated proposals. We may ask, does this structure apply to all DNA and at all times? The evidence that originally led to its formulation was the x-ray diffraction patterns of DNA fibers obtained by Wilkins and by Franklin (*17*). Such data, which arises from only the ordered regions of the fibers, provides information about only the ordered regions. Hence it can logically be said to apply only to that fraction of the fiber which is ordered. Estimates of this fraction range from 5 to 50 percent.

More conclusive evidence for the generality of a two-fibered structure is now available from the physical-chemical studies of Thomas (*18*) and of Schumaker, Richards, and Schachman (*19*). Both groups conclude from studies of the changes in light-scattering or in viscosity during enzymatic degradation of DNA that the great bulk—more than 90 percent—of their preparations must have been in the form of double chains.

In addition, the generally found near molar equality of adenine and thymine and of guanine and cytosine (*20*) is very neatly explained by this structure.

However, all the x-ray and physical studies with which I am familiar have been made on DNA from mature cells, such as thymus or DNA from cells with a migratory mission, sperm or phage. I think it would be premature to suggest that DNA is at all times in the life of the cell in this form. Indeed, there are sufficient reports of DNA fractions (obtained by varied modes of fractionation) which do not have complementary base ratios (*21*), that I think there may be small but important exceptions hidden behind an over-all complementarity.

This matter of complementarity also deserves a closer look. In its simplest form, it would limit the composition of DNA to four kinds of nucleotides. In fact, many, if not most, DNA's studied have five types (*22*). Most of the natural variants involve a perturbation upon the five position of cytosine.

In general, when such variants occur, the molar proportion of cytosine plus the substituted cytosine equals the molar proportion of guanine. However, the modified cytosine does not appear to be randomly introduced in exchange for cytosine. Studies of the dinucleotides obtained by the action of pancreatic deoxyribonuclease on thymus DNA (*23*) indicate a considerable difference in the distribution of cytosine and 5-methylcytosine (Table 2). It is hard to envision how such a distribution can be explained by a replication scheme guided by simple complementarity.

A more conclusive argument against a simple complementarity mechanism of replication arises from the following data. In T2 bacteriophage there is no cytosine—it is replaced by 5-hydroxymethylcytosine (HMC). Furthermore, about 77 percent of this 5-hydroxymethylcytosine is substituted by glucose. Now the DNA of T2 bacteriophage has been shown by Levinthal (*16*) to consist of one large piece, comprising about 40 percent of the DNA and a number of considerably smaller pieces. Brown and Martin have shown (*24*) that it is possible to fractionate DNA from T2 bacteriophage chromatographically into two fractions, and one of these corresponds to Levinthal's large piece. In addition, they have shown (*25*) that the 5-hydroxymethylcytosine lacking glucose is confined to the large piece—that is, only about 60 percent of the large piece is glucose-substituted, while all of the glucose of the small pieces is so substituted. Since these components of T2 DNA are all replicated in the same cell at the same time, the limited glucose substitution of the large piece cannot reasonably be ascribed to some metabolic limitation. Hence it would appear (to put the matter mechanistically) that when the replication of the large piece takes place, the machinery knows when to put in glucose-substituted 5-hydroxy-

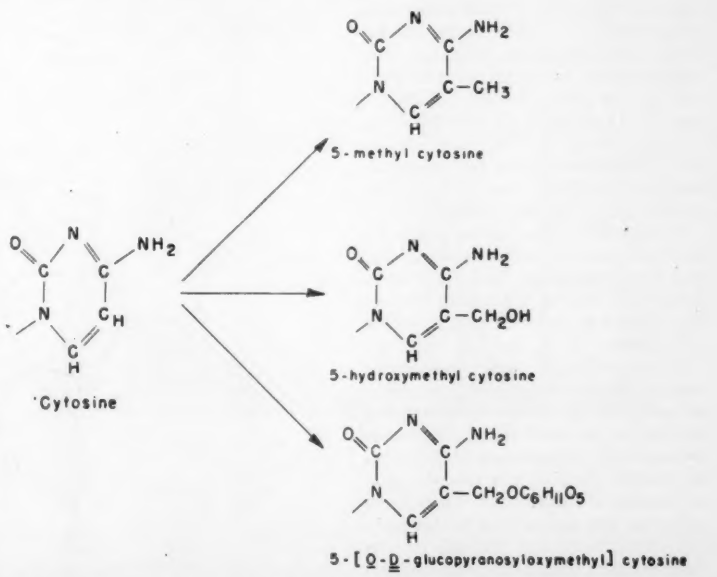

Fig. 3. Cytosine and the various substituted cytosine rings found in some DNA preparations.

methylcytosine or when to insert unsubstituted 5-hydroxymethylcytosine, for the glucose content remains unchanged through many generations.

To me, then, it appears that these perturbations of the nucleotides are significant and that replication of DNA involves a more precise mechanism than of simple complementarity.

Ultraviolet Spectra

The next piece of indirect evidence that I have cited for the association of DNA with the gene is the correlation of the ultraviolet action spectra for production of mutations in various organisms with the general shape of the ultraviolet absorption spectra of nucleic acids (*26*). To go beyond this simple correlation is certainly hazardous. We do not know what, physically, constitutes a mutation. Nor are we as yet very clear about what happens to DNA after the absorption of an ultraviolet photon.

As I indicated in the previous section, we suspect that the information content of a DNA molecule is contained in the sequence of its nucleotides. We know painfully little concerning such sequences. Most physical measurements suggest that DNA preparations as generally obtained consist of double chains varying in molecular weight from a few millions to several tens of millions—that is, of chains varying from a few thousand to tens of thousands of nucleotides. All DNA preparations to date have undoubtedly consisted of a mixture of a great many such molecules. One calf thymus nucleus would contain several hundred thousand of such molecules, presumably of many, many species. Hence any information obtained about sequence from such a preparation could only be of a statistical nature. A limited amount of information is available (*23*), such as is shown in Table 3, which lists the molar proportions of the various dinucleotides isolated from a deoxyribonuclease digest of calf thymus DNA.

It is possible in this way to specify the nucleotide sequence about some 10 percent of the phosphate links. I am confident that it will be possible to increase this fraction to 30 or 40 percent within a few years.

To proceed much further in sequence studies, which we expect will surely be necessary for the further understanding of mutation, we must be able to provide homogeneous preparations of DNA, as the protein chemists can now do with, say, insulin or ribonuclease. There seem to be two approaches open to this problem. One is to attempt to fractionate the components of these mixtures. Considerable effort is being expended upon such fractionation, and some success (*10, 27*) has been obtained (Fig. 5). The actual basis of these empiric fractionations is, however, still not understood.

The other approach would be to seek a biological system in which there were only a few—or ideally, one—type of DNA molecule. The viruses are the obvious choice for such an approach, and among these, the smaller the better. We have recently isolated a bacterial virus with a DNA content of about 2 million per particle—some 3000 nucleotide pairs. We do not as yet know whether the DNA is in one piece, but in any event, this virus should provide the closest approach yet to a homogeneous DNA, and sequence data upon its DNA may begin to acquire more than statistical significance.

If we believe that mutation consists of a change in nucleotide sequence, then we might inquire whether it could be possible to induce specific types of genetic alteration by the introduction of specific kinds of changes in nucleotide composition. Thus one can substitute 5-bromouracil for thymine and, as Litman and Pardee, and Zamenhof *et al.*, have shown (*28*), this is a highly mutagenic device. Whether the mutations induced are actually the product of specific tampering with the thymine residues or

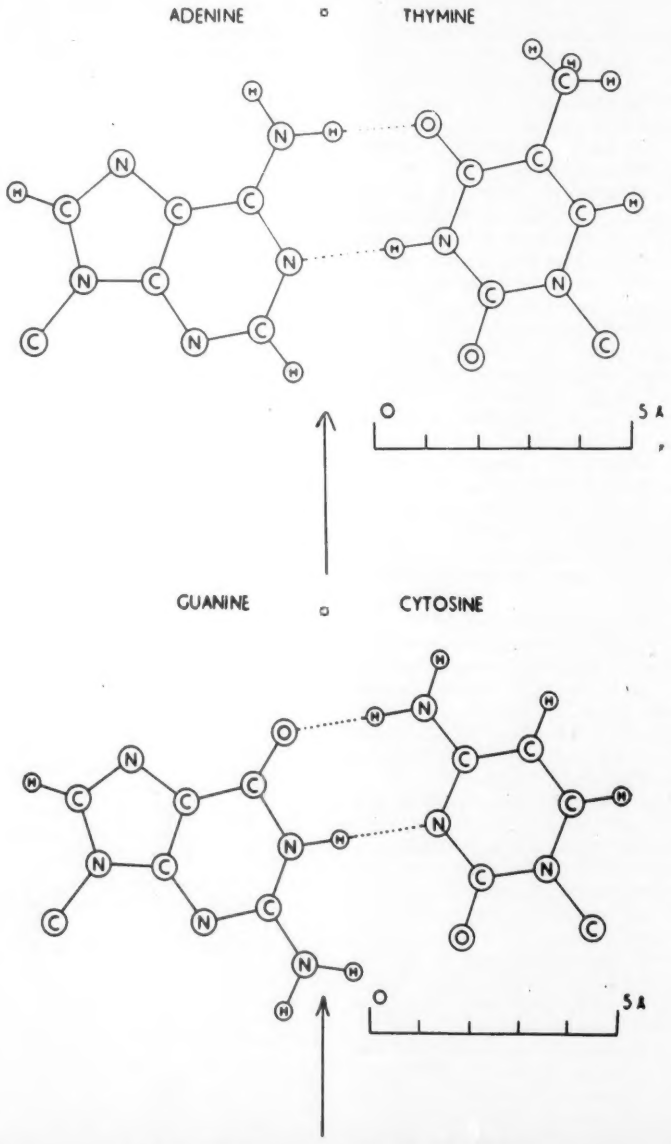

Fig. 4. The complementary base pairs of DNA.

Table 2. Comparison of the distribution of deoxycytidylic acid (C) and 5-methyldeoxycytidylic acid (M) among the dinucleotides obtained from calf thymus DNA by digestion with pancreatic deoxyribonuclease.

C-Dinucleotide	Mole fraction of digest	M-Dinucleotide	Mole fraction of digest
C-p-C-p-	1.11	M-p-M-p-	0
C-p-T-p-	0.78	M-p-T-p-	0
T-p-C-p-	2.34	T-p-M-p-	0
C-p-A-p-	0	M-p-A-p-	0
A-p-C-p-	3.22	A-p-M-p-	0
C-p-G-p-	0.75	M-p-G-p-	0
G-p-C-p-	0.12	G-p-M-p-	1.03

whether they are merely a general result of perhaps upsetting the pace of DNA synthesis remains to be determined.

We have some reason to believe that the effects of ultraviolet radiation will be to some extent localized to the cytosine residues (*29*). Such irradiation then may, under favorable circumstances, provide a specific kind of altered nucleotide sequence. Further understanding of genetic chemistry will almost certainly lead to more specific means of producing genetic modifications.

Transformation

As we now consider, briefly, the more explicit lines of evidence it will be wise to keep in mind that these all are, at present, demonstrable only with microorganisms and so their generality is thus unproved, even if often assumed.

The now classic tale of the transforming factor must be well known. Exposure of cells of strains of certain types of microorganisms to pure DNA from related donor strains which have distinguishing immunological or biochemical characteristics can result in the permanent acquisition by the first strain of the phenotypic character of the donor strain. Furthermore, the DNA of the transformed strain then has the power to pass the acquired characteristic on to still other strains (*30*). Studies involving the simultaneous transfer of two or more characteristics have shown the possibility of linkage which will again persist in the DNA of the transformed strain. This linkage must be thought to reside in the molecules of the DNA preparation (*31*).

That the DNA accomplishes this transformation by actual entry into the transformed cell has been shown by the elegant tracer studies of Goodgal and Herriot (*32*), and indeed they have obtained the pleasing result that on the average, per specific transformation, an amount of DNA equivalent to the DNA complement of one cell must enter the transformed cell.

Physically these DNA preparations with transforming power are no different than those prepared from varied sources. Indeed, the availability of a functional DNA has been of the greatest value, for assay of its biological activity has enabled one to assess the effects of various types of preparatory procedures, storage conditions and so on, on DNA.

When examined more closely, the phenomenon of transformation raises a great many questions, as has been thoughtfully discussed in several papers by Hotchkiss and by Harriet Ephrussi-Taylor (*33*). In solution, a DNA molecule is a greatly extended coil, which pervades a volume some 5000 to 10,000 A in diameter. How does such a molecule get into a bacterial cell, and indeed what is its physical state within the cell? Hotchkiss has shown (*34*) that it is only at certain stages of the mitotic cycle that the cells are ready to receive such molecules, but we do not understand their mode of entry.

And after the foreign DNA enters the cell, what accommodation is made with the indigenous DNA? Most likely some type of recombination process occurs. The occurrence of allogenic transformations which result in cells with new characters, distinct from those of either recipient or donor strains, suggests this very strongly. If transformation is by recombination, then how large a DNA piece must be exchanged between recipient and donor? It is conceivable that a few nucleotides at the right locus might be adequate.

I mention these matters merely to indicate that while the ability of DNA preparations to produce hereditable metabolic modifications is a striking phenomenon, our ignorance of the accompanying intracellular phenomena gravely limits the conclusions to be drawn.

Table 3. Molar proportions of dinucleotides in thymus DNA digest. M, 5-methyldeoxycytidylic acid; C, deoxycytidylic acid; T, thymidylic acid; A, deoxyadenylic acid; G, deoxyguanylic acid. *XY* = *X*-p-*Y*-p, where *Y* refers to the nucleoside carrying the phosphate monoester group in each case.

X/Y	M	C	T	A	G
M	0		0	0	0
C		1.11	0.78	0	0.75
T	0	2.34	1.38	0.10	0.16
A	0	3.22	1.36	0.46	0.97
G	1.03	0.12	2.61	0.20	0.82

Viral Infection

The role of nucleic acid in viral infection is best established for the T2 bacteriophage. Hershey's careful experiments have shown that, after attachment of the virus to the cell membrane, the DNA of the virus particle penetrates the cell wall while at least 97 percent of the protein remains external to the cell and appears to play little if any role in the subsequent development of the phage (*35*). If, as is commonly done, we chose to disregard the ambiguous 3 percent of protein, then we must conclude that the inherited properties of the virus are passed from generation to generation through the nucleic acid. Indeed, many varied pieces of information are most conveniently explained if we simply state that the action of the virus is to intro-

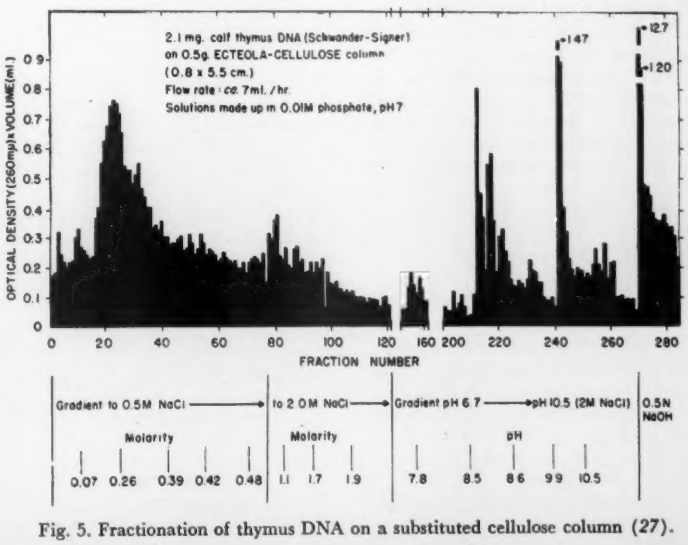

Fig. 5. Fractionation of thymus DNA on a substituted cellulose column (*27*).

duce its own genome, which, anthropomorphically put, destroys the bacterial genome and takes over the cellular control, directing it, of course, specifically to the synthesis of new virus. This concept neatly explains such observations as the ability of phage-infected thymineless mutants to synthesize thymine (*36*), the appearance of the new base, 5-hydroxymethylcytosine, and so forth.

We should note that with some of the other bacterial viruses the situation may be less simple. These viruses may be more dependent on the function of some of the bacterial genes and indeed there exists presumptive evidence for the recombination of the DNA of some viruses with the host DNA (*37*). Doubtless there are many degrees of molecular parasitism.

Bacterial Mating

That bacterial mating is on such a time scale that it can be conveniently interrupted and the transfer of genetic information placed on an accurate time scale has been brilliantly demonstrated by Jacob and Wollman in France and Skaar and Garen in this country (*38*). Thus, by mixing two genetically marked strains of crossable bacteria and by disruption of the union at various times after mixing by the action of a blender, it has been possible to show that gene A enters from the donor cell to the recipient at 12 minutes, gene B at 15 minutes, and so forth. And the order of entry of genes is just that order which has been deduced for the order of genes along the chromosome from mapping experiments. Similar results have been obtained by Skaar and Garen using a virus-susceptible donor, and employing phage to disrupt the mating.

That, as the genes enter, DNA enters, can be shown nicely by use of phosphorus-32 labeled donors, and this has been done. The amount of phosphorus-32 transferred, as shown both physically and biologically, is found to correlate in a general way with the fraction of the genome which has entered the recipient cell.

Conclusion

This concludes the most essential evidence. If now we will concede the point —if we acknowledge that these links between DNA and the hereditary factors are good and sound and enduring, we may face ahead and ask how shall we proceed to create a genetic chemistry—and the answer is, of course, on many fronts. Particularly, I think, we may ask what differentiates the DNA of different alleles. This is a structural question and hopefully will soon be susceptible to attack, and this in turn may lead to the linkage of structure with function. Also we may note that DNA is most certainly not to be found alone in the cell, and we may ask with what is it associated—and how these associations change during the cycle of mitosis, and we may hope that these associations may provide hints to help us discover how the information built into the DNA is passed on in duplication and is passed out to guide the metabolism of the cell.

To those who may have been chafing because I may seem to have equated DNA with the gene, let me hasten to say that I am confident that further experimentation will emphasize the interplay of protein and of ribosenucleic acid with DNA in the expression of the hereditary characters. And for those for whom the term *hereditary factor* itself has become fuzzy, let me hope that the development of a genetic chemistry will help to illuminate both the gene and the problem of its definition.

I believe this hard-won recognition of the role of DNA has brought us into a new era in genetics and in biochemistry. The gene, once a formal abstraction, has begun to condense, to assume form and structure and defined reactivity.

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Smoking and Health

Joint Report of the Study Group on Smoking and Health

The Study Group on Smoking and Health was organized in June 1956, at the suggestion of the American Cancer Society, the American Heart Association, the National Cancer Institute, and the National Heart Institute, to review the problem of the effects of tobacco smoking on health and to recommend further needed research to the sponsoring organizations.

The study group has held six 2-day conferences, has examined the pertinent literature and more recent unpublished reports, and has consulted with scientists representing specialized areas of research concerned with the subject.

The study group, cognizant of the implications of its conclusions and recommendations, now submits the following joint report.

Lung Cancer

At least 16 independent studies carried on in five countries during the past 18 years have shown that there is a statistical association between smoking and the occurrence of lung cancer (appendix A). (As used in this report, the term *lung cancer* refers to epidermoid and undifferentiated types of carcinoma of the lung, but not to adenocarcinoma.) These retrospective studies have been reinforced by two investigations in which large male populations have been followed prospectively. Lung cancer occurs much more frequently (5 to 15 times) among cigarette smokers than among nonsmokers, and there is a direct relationship between the incidence of lung cancer and the amount smoked. It is estimated that on a lifetime basis, one of every ten men who smoke more than two packs a day will die of lung cancer. The comparable risk among nonsmokers is estimated at one out of 275 (appendix B). Self-selection and sampling bias have been mentioned as possible sources of error. Examination of the evidence shows that any distortion resulting from these sources does not invalidate the conclusions (appendix C).

Epidemiologic studies also indicate that cigarette smoking cannot account for all cases of epidermoid cancer of the lung. There are other causative environmental factors, the most important of which are probably various atmospheric pollutants. As in other diseases, various other influences, such as sex, nutrition, and heredity, may modify its occurrence (appendix D).

The two prospective studies further suggest that cessation of smoking by chronic smokers decreases the probability that such individuals will develop lung cancer.

The epidemiologic evidence is supported by laboratory studies on animals. At least five independent investigators have produced malignant neoplasms by tobacco smoke condensates. Although the active material has not been identified chemically, some progress has been made in localizing the activity in purified fractions (appendix E). Although the demonstration of carcinogenic activity in animals does not constitute proof of carcinogenicity in the lungs of human beings, this is important contributory evidence that strengthens the concept of causal relationship.

Studies on pathogenesis of human lung cancer are also compatible with the causal relationship. Physiologic observations indicate that foreign material is trapped in the tracheobronchial tree, particularly where ciliary action is inhibited or the ciliated epithelium is destroyed (appendix F).

Fluorescent substances present in cigarette smoke have been shown to enter the cells of the buccal mucosa (appendix G). Detailed histologic studies of the tracheobronchial tree indicate that basal cell hyperplasia, atypical hyperplasia, squamous metaplasia, and areas of morphologic alteration with all characteristics of carcinoma *in situ* are encountered more frequently among cigarette smokers than among nonsmokers (appendix H). Thus, every morphologic stage of carcinogenesis, as it is understood at present, has been observed and related to the smoking habit.

The sum total of scientific evidence establishes beyond reasonable doubt that cigarette smoking is a causative factor in the rapidly increasing incidence of human epidermoid carcinoma of the lung.

The evidence of a cause-effect relationship is adequate for considering the initiation of public health measures. Nevertheless, additional research is needed to clarify many details and to aid in the most effective development of a program of lung cancer control. The need for information in the following areas appears to be very important: (i) the isolation, identification, and possible elimination from tobacco smoke of chemicals that produce cancer in animals (appendix I); (ii) the role of atmospheric pollutants and additional environmental factors other than cigarette smoking in the causation of lung cancer in man; (iii) the effect of cessation of smoking on the occurrence of lung cancer in man (appendix J); (iv) measurement of possible physiologic, sociologic, and psychologic differences between smokers and nonsmokers and the relation of host differences to the occurrence of lung cancer (appendix K).

Longevity and Cardiovascular Diseases

At least three statistical investigations show an association of tobacco smoking with a decrease in longevity, probably referable to a higher risk, for male smokers, of dying from cardiovascular disease. The mortality among smokers in certain age groups is reported to be approximately double that of the nonsmokers (appendix L).

The study group is of the opinion that the significance of this observation requires further research before its meaning can be determined. Cardiovascular diseases account for well over half of all adult male deaths. Even a relatively small proportionate excess in the cardiovascular death rate could, therefore, contribute a larger number of deaths than a much larger excess in the lung cancer death rate.

In the few reports available, there is no convincing biological or clinical evidence to indicate that smoking per se has a causative role in cardiovascular disease. Many physicians have the clinical impression that patients with coronary artery disease should not smoke, on

Members of the Study Group on Smoking and Health, which was sponsored by the American Cancer Society, the American Heart Association, the National Cancer Institute, and the National Heart Institute, are Frank M. Strong, University of Wisconsin, Madison, *chairman*; Richard J. Bing, Washington University Medical School, St. Louis, Mo.; Rolla E. Dyer, Emory University Medical School, Atlanta, Ga.; Abraham M. Lilienfeld, Roswell Park Memorial Institute, Buffalo, N.Y.; Norton Nelson, Postgraduate Medical School, New York University, New York; Michael B. Shimkin, National Cancer Institute, Bethesda, Md.; and David M. Spain, Beth-El Hospital, Brooklyn, N.Y. Dean F. Davies of the American Cancer Society assisted the group as executive secretary.

the basis that smoking may be detrimental to previously damaged coronary arteries. A few studies have provided some validating evidence for this hypothesis. However, further systematic investigation is essential (appendix M).

The study group strongly urges a research program of wide scope that will clarify the relationship and association between smoking and cardiovascular diseases. The following areas are considered to be of particular importance: (i) epidemiologic studies, with appropriate consideration of the roles of other factors such as diet, physical activity, and blood lipides (appendix N); (ii) the chronic effects of tobacco and nicotine in animals, with and without experimental atherosclerosis; (iii) further physiologic studies of man, particularly of the effect of smoking on coronary artery blood flow in normal individuals and in individuals with coronary insufficiency.

Other Diseases

The study group considered reports of association of smoking with a number of other disease entities, including carcinoma of the larynx, oral cavity, esophagus, bladder, and stomach; peptic ulcer; bronchitis and tuberculosis; and thromboangiitis obliterans (appendix O).

The evidence that relates smoking directly to thromboangiitis obliterans is based on repeated, well-confirmed demonstrations that the disease is materially ameliorated by cessation of smoking and strikingly aggravated by continued smoking (appendix P).

For the other conditions mentioned, the relationships have been studied only to a degree that indicates statistical association. Further research on the individual conditions is necessary before valid conclusions can be drawn.

Conclusions

The study group concludes that the smoking of tobacco, particularly in the form of cigarettes, is an important health hazard. The implications of this statement are clear in terms of the need for thorough consideration of appropriate control measures on the part of the official and voluntary agencies that are concerned with the health of the people. The lack of specific recommendations in this regard reflects no lack of interest. Rather, it reflects the desire of the study group to limit its recommendations to the area of research needs in accordance with the instructions it received.

The study group recommends that further research on smoking and health be vigorously pursued. The recommendations made in the section on "Lung cancer" are for research into means of coping with lung cancer hazard, which has been established for cigarette smoking. The recommendations of the sections on "Longevity and cardiovascular diseases" and "Other diseases" are directed primarily at establishing whether smoking is one of the contributory factors in other diseases, particularly in coronary artery disease. Many of these answers can best be obtained by a cooperative research effort.

The Study Group on Smoking and Health approves dissemination of this report as desired by the sponsoring agencies and hereby terminates its activities.

Appendixes

A) Fourteen (*1–14*) of the retrospective studies have been reviewed by Cutler (*15*). Stocks and Campbell (*16*) have studied the association between smoking and lung cancer in terms of place of residence. An additional recent retrospective study by Wynder (*17*) is concerned with the occurrence of lung cancer in women.

B) Doll and Hill (*18*) in England and Hammond and Horn (*19*) in this country reported their first results in 1954. Since then, Doll and Hill have published a follow-up report (*20*), and Hammond has reported additional data (*21*).

Although the statistical evidence has often been quoted as indicating an association between *heavy* smoking and lung cancer, there is no evidence of a threshold level below which the risk disappears. The best available estimates for both the United States and England indicate that the lung cancer risk is statistically significant for half-pack-a-day smokers and that there is a correlation of risk with amount smoked (*16, 20, 21*).

C) By numerical illustration, Berkson (*22*) has indicated that, in epidemiologic studies similar to the one conducted by Hammond and Horn (*19*), it is possible to obtain a spurious statistical association between smoking and a disease as a result of sampling bias, even though no real association exists. It has been pointed out by Cornfield (*23*), Korteweg (*24*), Levin (*25*), and Lilienfeld (*26*) that, in order for the degree of association between cigarette smoking and lung cancer observed by Hammond and Horn to be a result of sampling bias, it would be necessary to assume an unreasonably large degree of such bias. Furthermore, a study of smoking habits of a probability sample of the United States population reported by Haenszel and associates (*27*) indicates that the necessary degree of sampling bias was not present in the Hammond-Horn study. Berkson also indicated that the influence of sampling bias would disappear with the passage of time. Doll and Hill (*20*) have recently reported that, over a 4-year period of observation, the gradient of lung cancer mortality in relation to the amount smoked has remained remarkably constant during each of the 4 years.

The issue of self-selection is raised as an argument against interpreting the statistical association of cigarette smoking and lung cancer as a causal relationship. Self-selection assumes that there is a factor that both causes a person to smoke and causes lung cancer; thus, individuals are selected for both smoking and lung cancer by a third mutually related factor. Such a hypothesis does not appear likely. Doll and Hill (*20*) and Levin (*25*) have indicated that such a hypothesis would be inconsistent with the marked increase of lung cancer mortality in recent years. The likelihood of this hypothesis is diminished further by the biological and pathogenetic evidence discussed in this statement. However, information concerning the characteristics of smokers and nonsmokers would be valuable for further evaluation of this theoretical possibility.

D) Epidemiologic studies indicate that cigarette smoking cannot account for all cases of lung cancer; nonsmokers do develop lung cancer, and variations in frequency of lung cancer in different population groups are not completely related to variations in frequency of cigarette smoking. The most significant observation on this point is the higher death rate from lung cancer in urban, as compared with rural, areas (*28, 29*). This excess urban death rate has been attributed by most investigators (*16, 30, 31*) to the probable influence of air pollution. As has been indicated by Hammond (*29*) and by Haenszel and Shimkin (*28*), part of this urban excess may be attributed to the higher proportion of cigarette smokers among urban populations, but they have also pointed out that even after adjustment has been made for differences in smoking habits, the urban rate is still higher than the rural rate. Estimates have been made of the relative contribution that cigarette smoking and the "urban factor" (probably air pollution) make to the lung cancer deaths. From studies in Liverpool, Stocks and Campbell (*16*) have estimated that 50 percent of the lung cancer deaths result from smoking and about 35 percent from air pollution. Hammond (*29*) estimated that about 31 percent of lung cancer deaths are due to air pollution. It is recognized that these estimates may not be very precise, but they do afford some idea of the relative importance of these two factors. Recently, Hueper (*30*) and Kotin (*31*) have defended their views that air pollution is the *major etiologic factor* in

lung cancer and that cigarette smoking plays a minor role, if any. Cigarette smokers have higher lung cancer death rates than nonsmokers in urban areas, where presumably both of these groups have had similar exposure to general air pollution. A definite need exists for determining the chemical nature of these pollutants and estimating more precisely the role of air pollution, particularly in relation to the effect of cigarette smoking.

Several studies indicate that occupational exposure to chromate ore (*32*), radioactive dust, and other agents (*30*) increases the risk of lung cancer. However, specific occupational exposures have been demonstrated to be responsible for only a small percentage of lung cancer deaths.

It is also possible that additional factors increase host susceptibility to these environmental factors. There is suggestive evidence that hormonal factors may have some influence (*33*). The possible existence of endogenous factors that influence susceptibility to exogenous agents should be further investigated, since such information may have some bearing on control efforts.

E) In addition to the five recent demonstrations of carcinogenic activity in tobacco smoke (*34–38*), Roffo (*39*) and Woglom (*40*) had previously reported the production of cancers from tobacco tar. Evidence for a cocarcinogenic effect of tobacco smoke condensate has been obtained by Gellhorn (*41*).

Several workers have now reported the presence of 3,4-benzopyrene in tobacco smoke (*42–46*). This has been demonstrated to be present in the neutral fraction of tobacco smoke condensate at concentrations of about 2 micrograms per 100 cigarettes. According to Wynder (*47*), the concentration is so low that the biological activity observed in his most purified fractions cannot be the result solely of 3,4-benzopyrene. Other carcinogenic polycyclic hydrocarbons are being sought. In addition to 3,4-benzopyrene, Bonnet and Neukomm (*43*) found other polycyclic hydrocarbons, including 3,4,9,10-dibenzopyrene at an estimated concentration of 1 microgram per 100 cigarettes.

Recently Lacassagne, Buu-Hoi, and others (*48*) produced sarcomas in mice by three subcutaneous injections totaling 1.8 milligrams of this compound per animal. The quantitative aspects of this problem obviously should be investigated.

F) In the normal human lung, particulate matter, upon inhalation, may penetrate diffusely throughout and into the alveoli. This is evident from many observations, both clinical and experimental. O. H. Robertson (*49*), in an exhaustive investigation and review of this subject, presents evidence to indicate that such factors as particle size and concentration and the depth of ventilation, as well as time of exposure, are important determinants of the amount of particulate matter that will enter the lung. It is estimated that the range of particulate size in cigarette tobacco smoke is between 0.3 and 1.0 microns. Particles of this size, upon inhalation, may readily be distributed diffusely throughout the lung.

Increased depth of ventilation, such as is seen in inhalation during smoking, favors the entrance of greater amounts of particulate matter into the lungs. Particles that penetrate the upper air passages come in contact with the mucus-covered surface of the bronchi, where they tend to adhere and to remain in contact with bronchial mucosa for varying periods of time, depending on the size and nature of the particles.

An irritant such as smoke may bring about alterations in the ciliary activity of the bronchial mucosa. It is this ciliary activity that is the main mechanism available for the removal of particulate matter from the lung (*50*). Slight temporary alteration in this ciliary activity will allow for the retention of particulate matter. Furthermore, any alteration in the quantity or quality of mucus in the tracheobronchial tree will also interfere with the removal of particulate matter. Particles may become concentrated in outdrifting mucus and remain in contact with bronchial mucosa for significant periods of time. Hilding (*51*) demonstrated the possible role of paralyzed cilia or deciliated areas in the accumulation of cigarette tar by exposing recently removed calf lungs to cigarette smoke.

G) After smoking, according to the degree of keratinization, some chronic cigarette smokers who were tested were found by Mellors (*52*) to have fat-soluble fluorescent substances in scrapings of the buccal mucosa. Such substances are not observed, to any appreciable degree, 12 hours after smoking.

H) It is well established that changes may be observed in epithelial surfaces that precede established forms of invasive carcinoma. These alterations consist of atypical hyperplasia, metaplasia, and carcinoma *in situ*. Although there may be disagreement in the terminology in these early morphologic changes, their presence and significance are generally accepted. It has been demonstrated by Black and Ackerman (*53*) that epidermoid carcinoma *in situ* is an important stage in the histogenesis of lung cancer. If smoking is related causally to the development of epidermoid carcinoma of the lung, then one would expect to find a greater incidence of these early morphologic changes in the bronchial tree in smokers than in nonsmokers. A study investigating this hypothesis was carried out by Auerbach and associates (*54*).

A total of 28,638 slides was made from the tracheobronchial tree of 150 autopsied individuals in whom a cigarette-smoking history had been obtained. Such changes as basal cell hyperplasia, stratification, squamous metaplasia, and carcinoma *in situ* were found, both quantitatively and qualitatively, to a significantly greater degree in smokers than in nonsmokers. The findings were accentuated in autopsied cases of bronchogenic carcinoma; all such patients had been smokers. Carcinoma *in situ* was found in 1 percent of the slides of those who did not smoke regularly whereas it was found in 6 percent of the slides in those individuals who smoked more than one pack of cigarettes a day. Determination of the incidence of the various stages of these lesions, as related to sex, age, and exact anatomic distribution, awaits the investigation of larger numbers of cases. The alterations recorded by Auerbach were similar in almost all details to those that are found to precede and develop into epidermoid carcinoma of the uterine cervix.

Chang (*55*) and Chang and Cowdry (*56*) studied whole amounts of bronchial epithelium obtained at autopsy from smokers and nonsmokers. They found metaplasia and thickening of the epithelium more common among the smokers than among the nonsmokers. These results are in good agreement with those of Auerbach. In addition, they observed that the cilia were shorter and that Goblet cells were more numerous in the lungs of smokers than in those of nonsmokers.

I) It is possible that an innocuous cigarette could be developed without prior identification of the active agents, and efforts along this line should parallel the work on characterization of the active materials. However, if empiric reduction is achieved, it would still be urgent to define the chemical nature of the agents and their mode of action.

Reduction in tumor activity might be sought by the removal or inactivation of carcinogenic, cocarcinogenic (promoting) factors or the precursors of either. Possibilities that suggest themselves include selection of tobacco strain, extraction of tobacco leaves, alteration of the burning temperature of the cigarette, and, possibly, selective removal of the active material from tobacco smoke. In this connection, it should be noted that the filters that are presently in use do not appear to be selective in their action; rather, they reduce tumor activity only to the extent that they remove whole smoke (*47*). In the case of most commercial cigarette filters, efficiency is not high, and accordingly the

amount of smoke that reaches the lungs is not reduced to any major degree.

An incidental but urgent requirement for the identification studies is improved assay procedures, since the work is at present hampered by the necessity for relying on slow and relatively insensitive methods.

J) The most desirable method of obtaining information concerning the effect of cessation of smoking would be by an experiment with human beings. A description of one of several designs follows. A group of smokers, who would volunteer to be included in the study, would be randomly allocated to an experimental and a control group. The control group would continue to smoke, whereas the experimental group would be asked to give up smoking. These groups would be followed for a number of years to determine the risk of dying, in general, and the risk for specific causes of death. Even though all individuals in the experimental group had not ceased smoking, comparisons of mortality rates in the two groups would be made. Obviously, success of the experiment would depend on the proportion of the experimental group who had stopped smoking; if it is 50 percent or more, meaningful results could be expected.

Consideration of sample sizes required for this experiment indicated that very large samples would be necessary to obtain results with respect to lung cancer because of the relatively low death rate from this cause. However, the estimated sample sizes for studying the effect of cessation of smoking on total mortality, particularly on death from cardiovascular disease, appeared to be within practical limits; at least, they were such that further exploration of the feasibility of such an experiment appears warranted. Prior to conducting a full-scale experiment, a pilot study should be undertaken. Such a study is important, not only from a biological viewpoint but also from a public health administrative viewpoint, in that it would be a means of evaluating the feasibility of certain control efforts.

It should be recognized, of course, that such an experiment would fail to show a difference between experimental and control groups if the damage to the organ system had been irreversibly established at the time smoking was stopped.

Further information on the effect of cessation can be obtained from the prospective studies of Hammond, Doll and Hill, and from the Veterans' Study that is now being conducted by the National Institutes of Health, It is recommended that collection of the necessary data continue to be made with respect to this aspect of these studies.

K) A large prospective study of the effect of smoking on lung cancer and other causes of death among approximately 220,000 veterans of World War I is now in progress, at the National Institutes of Health, under the direction of Harold F. Dorn. This study offers an excellent opportunity to explore, by additional questionnaires and interviews, some of the possible differences that may exist between smokers and nonsmokers. In addition, this study could also be expanded to include cardiovascular evaluation, perhaps even to the extent of including physical examinations and laboratory determinations on subsamples of the smoker and nonsmoker groups.

The study group has been in contact with Dorn and has suggested that additional questionnaires and clinical and laboratory determinations might be valuable. It is hoped that these suggestions will be developed into research actions with the help of the National Heart Institute and the U.S. Veterans Administration.

There is no evidence at present to indicate that the occurrence of cancer of the lung among cigarette smokers is limited to an undefined subgroup of susceptible individuals. Nevertheless, certain characteristics may well be correlated with greater or less susceptibility to lung cancer or heart disease. Research on host factors that may be associated with, or modify, certain disease states is of great importance. This is particularly true of chronic diseases in which the etiologic situations are often multiple and in which the host response may play a paramount role.

L) Pearl (*57*), Hammond and Horn (*19*), and Doll and Hill (*20*) have all shown an increase in mortality associated with smoking. Pearl found the mortality rate for all causes among cigarette smokers to be just twice that of nonsmokers among men from 60 to 65 years of age. In the same age group, Hammond and Horn reported a ratio of 1.9. Doll and Hill found that the mortality rate increased progressively with the amount smoked, so that heavy smokers for all age groups over 35 had a mortality rate 42 percent higher than nonsmokers.

For coronary artery diseases, Gertler and White (*58*) studied smoking habits, results of which showed a significantly higher number of smokers among the heart patients than among controls. English, Willius, and Berkson (*59*), in 1940, found a greater incidence of coronary disease in male smokers than among nonsmokers, particularly at ages under 50. Hammond and Horn (*19*) found that the death rates from coronary artery disease for men who smoked a pack or more of cigarettes a day were more than twice as high as the rates for men who had never smoked; this is true for age groups from 50 to 65. The findings of Doll and Hill (*20*) on death from coronary thrombosis "agree broadly with those of Hammond and Horn," but the increase is less marked.

M) Evidence that points to the effect of nicotine on the coronary circulation was obtained by Bargeron and associates (*60*), who found that cigarette smoking increases the coronary blood flow in individuals who do not have heart disease. That nicotine may cause a decrease in coronary blood flow if the coronary vessels are atherosclerotic has been suggested by ballistocardiographic studies. Davis and associates (*61*) have confirmed the reports of others that show definite ballistocardiographic abnormalities in patients with coronary heart disease; these alterations were not present in individuals with normal hearts.

Experimentally, Travell (*62*), at Cornell University, has demonstrated that nicotine causes a diminution in coronary blood flow in perfused hearts of rabbits that had previously been made atherosclerotic through dietary measures.

It is felt that one of the most pressing problems consists of direct investigation of the coronary circulation, during smoking, of patients with arteriosclerotic heart disease. The techniques for this investigation are being developed, but the present methods are not yet applicable.

N) In contrast to the studies of lung cancer, the number of studies concerned with the relationship of smoking to cardiovascular diseases have been relatively few. Most epidemiologic investigations of heart disease have been concerned with evaluating the etiologic role of diet, physical activity, and blood lipides. A definite need exists for both retrospective and prospective studies on smoking and heart disease. Several independent studies should be conducted in various parts of the country. Because of the possible influence of diet, physical exercise, and blood lipides, they should be taken into account to determine possible interrelationships of these factors with smoking. In addition, it is possible that studies of heart disease that are already in progress could be expanded to obtain further information concerning the effects of smoking. The study group considered that the Veterans' Study now being conducted by the National Institutes of Health offers an excellent opportunity for expansion to include the suggestions made here.

O) A few references to studies that relate smoking to some of these diseases should be noted. Lilienfeld, Levin, and Moore (*63*) demonstrated a statistical association between smoking and cancer of the urinary bladder and felt that it was highly suggestive of a cause-and-effect relationship. Friedell and Rosenthal (*64*) and Moore and associates

(*65*) have discussed the evidence for carcinogenic activity of unburned tobacco in producing oral cancers. Wynder (*66*) has reported some evidence that alcohol consumption increases a smoker's susceptibility to laryngeal cancer. The evidence regarding the etiologic role of smoking in gastrointestinal disease is highly controversial (*67, 68*).

Case and Lea (*69*) found an association between chronic bronchitis and lung cancer in World War I pensioners. Unfortunately, smoking histories were not available. However, Joules (*70*), Palmer (*71*), Oswald and Medvei (*72*), and Abbott and associates (*73*) found that chronic bronchitis was closely associated with heavy smoking (see *74*). Lowe (*75*) found that heavy smokers were significantly more common among tuberculosis patients than among control patients.

P) For references to the voluminous literature on this condition, see Allen, Barker, and Hines (*76*).

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H. N. Russell, Astronomer

The death of Henry Norris Russell on 18 February marks the passing of one of the most brilliant minds that has flourished in the modern scientific world. A scientist of truly remarkable breadth, he was for many years the leading theoretical astronomer in this country and a pioneer in the use of atomic physics for the analysis of stars.

Russell's astronomical career began, as it ended, at Princeton University, where he spent 62 of his 79 years. He entered Princeton with the class of 1897 and was graduated with the highest scholastic record of his generation. During the quarter of a century when Latin honors were awarded to high-standing seniors, he was the only Princeton undergraduate whose record was so outstanding that he was graduated *insigni cum laude*. His Ph.D. degree was obtained at Princeton 3 years later, under C. A. ("Twinkle") Young, his famous predecessor at the Princeton Observatory. After 2 years in Cambridge, England, he returned to Princeton University, where he rose rapidly up the academic ladder and became professor of astronomy in 1911, at the age of 33. The following year, he became director of the Princeton University Observatory, succeeding Young.

During his early years as an astronomer, Russell engaged in a number of programs, largely in such classical topics as stellar parallaxes, photographic positions of the moon, and celestial mechanics. In 1912 he turned to the analysis of stellar spectra, a subject in which he remained active throughout his career. The famous diagram of stellar luminosity against surface temperature, originated

by Hertzsprung, was used so extensively by Russell in his physical analyses of stars and in his theories of stellar evolution that this basic plot is generally referred to as the "Hertzsprung-Russell diagram." In the same year he published his analysis of the light curves of eclipsing variable stars. These double stars, whose light varies periodically because one star eclipses the other, had been known for some time, but no simple method existed for interpreting the observed light curves quantitatively. With a characteristic genius for handling complicated data, Russell devised a convenient and useful method for extracting full information from such observations. The method did not long remain untried. "For then," as Russell later used to remark, "the Lord sent me Harlow Shapley." This young Ph.D. candidate at Princeton, who was destined to become Russell's best known student, applied Russell's techniques to 87 double stars as his doctoral thesis. With the advent of photoelectric techniques, the observations are now much more accurate than they were 45 years ago, and more refined methods have been developed for certain types of binaries. However, Russell's method remains the standard one for a first interpretation of any eclipsing-variable light curve.

During World War I, Russell, like so many other scientists, became involved in military research. During the decade following the war, much of his time was spent in preparing a textbook on astronomy, in collaboration with his colleagues, R. S. Dugan and J. Q. Stewart. The first volume of this work was a revision of Young's *Manual of Astronomy,* but the second volume, dealing with modern astrophysics and stellar astronomy, was, for the most part, new. A great deal of effort went into the preparation of these two volumes. Virtually nothing was taken on faith, and much original research was carried on to provide material for the book. An indication of the thorough care that went into this textbook for undergraduates is the fact that, for almost three decades, "Russell, Dugan, and Stewart" remained a standard reference work, despite enormous advances in most astronomical fields.

It was, perhaps, the preparation of this general textbook that gave Russell the extraordinary knowledge of astronomy that was so characteristic of his mature years. An astronomer in any field could count on Russell's intelligent interest and helpful comments.

In 1924 he embarked on a research problem that was destined to take much of his time during the rest of his active life. In that year he published his first paper on the analysis of atomic spectra, a subject in which he became interested because of the pivotal importance of spectroscopy in astrophysics. During the next 10 years he published 25 papers in this new and exciting field of basic physics. A pioneer in this field, he originated, with Saunders, a theory for the coupling between spin and orbital momentum in atomic electrons. He took great delight in unraveling complicated spectra and in determining the atomic energy levels involved.

The years 1928–29 may be regarded as the apex of Russell's professional career. He was then just over 50 years of age and at the peak of his powers. Although immersed in the task of spectroscopic research, he carried on several other important analyses at about this time. His analysis, with Adams, of stellar spectra, appeared in 1928, and his great work, *On the Composition of the Sun's Atmosphere,* appeared in 1929. In these papers he used the Saha ionization equation to determine the pressure and chemical composition of stellar and solar atmospheres. He concluded, in variance with accepted beliefs, that hydrogen was overwhelmingly the most abundant element in the solar atmosphere. For many elements his values of relative abundances are still the best available, and his assertion of the great abundance of hydrogen has now, after a prolonged controversy, been accepted as one of the most basic facts of cosmology. During this same period he also published an analysis of the rotation of the line of apsides in eclipsing variables, in which he pointed out a very important method —in fact, the only observational method —for obtaining the density distribution in stars.

During his later years, Russell continued active research in all these fields. In addition, he maintained his lively interest in stellar evolution and planetary origin. His little monograph, *The Solar System and Its Origin,* did not present any new and sweeping theory but was of great help in clarifying the field and stimulated several of his students to productive work in this area.

On so outstanding a scientist, honors were showered from all sides. Medals were awarded him at various times by the Royal Astronomical Society (England), by the French Academy, by the National Academy of Sciences, by the American Academy of Arts and Sciences, and by the Astronomical Society of the Pacific. Honorary degrees were awarded him by Yale, Harvard, and Princeton universities, among others. He was a member of many learned societies and past president of several. In 1946, Mexico presented him with its highest award for foreigners, the Order of the Aztec Eagle.

There are few men now living who remember Russell as a young man. Those who knew him in his later years remember him for his unbounded energy and his enthusiasm for ideas. It is characteristic of the man that he would frequently be so carried away in his graduate lectures that he would talk enthusiastically for an additional hour or two, carrying his fascinated audience into exciting new realms of research. He brought this same keenness and enthusiasm to all the many experiences in his full and active life—to his extensive travels, his wide reading of both prose and poetry, and his happy hours with his grandchildren. He would keep small children engrossed for hours with the paper boats, balls, birds, and animals that he constructed with facility, his long, dexterous fingers folding and creasing the paper with unerring speed. His knowledge was encyclopedic; it included facts and theories not only in all branches of science but also in such varied subjects as the Bible and the wild flowers of New Jersey.

A deeply religious man, he was convinced that there was no basic conflict between science and religion. For several years he organized among the graduate students regular discussions of the interrelations between science and religion and published a little book on the subject, *Fate and Freedom.* Through his vast and cogent writings, through his many and vital discussions with colleagues and students, and through the sheer force of his personality and giant intellect and their impact on all who knew him, the influence of Henry Norris Russell will continue through many generations to come.

LYMAN SPITZER, JR.
Princeton University Observatory,
Princeton, New Jersey

News of Science

International Atomic Energy Agency

Postponement of the first general conference of the International Atomic Energy Agency until 1 Oct. has been announced by the preparatory commission. The meeting had been scheduled to start 19 Aug. The conference is to organize the new agency and make decisions on its program during its first year. The new date will insure sufficient time for participating governments to consider program proposals.

It is possible that the postponement was influenced by the failure of the United States and other atomic powers to ratify promptly the statute of the agency. The following states have so far deposited instruments of ratification with the Government of the United States, acting as depositary government: 29 Mar., Guatemala; 5 Apr., Switzerland; 8 Apr., Byelorussian S.S.R. and U.S.S.R.; 12 Apr., Romania; 2 May, Pakistan; 10 May, Austria. In order to come into effect, the statute must be ratified by 18 states, including three of the following five: Canada, France, the U.S.S.R., the United Kingdom, and the United States.

College Presidency Study

Harold W. Dodds, who retires this month as president of Princeton University, will direct a study of the office of the college and university presidency, with support from the Carnegie Foundation for the Advancement of Teaching. The foundation has announced that it has made a grant for this purpose to the Institute for College and University Administrators, Boston, Mass.

Dodds will begin work on the study, which will probably take 2 years to complete, on 1 Jan. of next year in New York City. He and a small staff expect to look into the historical development of the office in the United States and the nature of the college president's job today. Dodds will visit a number of campuses and will talk not only with presidents but with deans, faculty members, and members of boards of trustees.

In midsummer, after launching the preliminary phases of the study, Dodds will depart for Australia to accept a long-standing invitation of the Australian Vice-Chancellor's Committee. The committee annually invites a distinguished educator from overseas to lecture to Australian universities and to discuss general education problems with Australian educators. Dodds' visit will mark the first time that the Vice-Chancellor's Committee has invited its annual guest lecturer from outside of the Commonwealth. Dodds will arrive in Sydney in late August and will return to the United States sometime in December.

First-Generation Effect of Radiation

An experiment that was designed by W. L. Russell of the Oak Ridge National Laboratory to compare the genetic effects of neutrons from an atomic bomb with those from a cyclotron has led to some observations on the effect of neutron radiation on length of life [*Proc. Natl. Acad. Sci.* (*U.S.*) **43**, 324 (April 1957)]. Russell exposed male mice, shielded by 7-inch-thick lead hemispheres, to atomic bomb radiation. The lead shielding reduced the gamma-component of the bomb's radiation to such an extent that it would not seriously interfere with estimates of neutron effect. The exposed mice were crossed with untreated females and the offspring kept throughout their life-span. In a summary of his results Russell states:

"Length of life in the offspring of male mice exposed to moderate doses of neutron radiation from a nuclear detonation is shortened by 0.61 day for each rep received by the father over the dose range tested. . . . Extrapolating to a proportional shortening of life in man gives 20 days per rep received by the father as the point estimate and 5 and 35 days as the 95 percent confidence limits. . . . It seems likely that, even when allowance is made for the conditions of human radiation exposure, shortening of life in the immediate descendants will turn out to be of a magnitude that will warrant serious consideration as a genetic hazard in man." Russell attributed the shortening of life largely to the dominant deleterious effects of recessive lethal genes.

NSF In-Service Institutes

Grants totaling $138,000 have been awarded by the National Science Foundation to 18 colleges and universities in the United States and its territories to support in-service institutes designed to improve the training of high-school teachers of science and mathematics. In-service institutes will begin in the fall of 1957 and will run through the academic year 1957–58. Each will offer special courses in the subject matter of science or mathematics especially designed for the needs of high-school teachers.

Institutes will be held in the evenings and on weekends in order that teachers may attend them outside regular teaching hours. Travel expenses, tuition, and fees for each participant will be covered by the grant from the National Science Foundation. Participants in each institute will be selected from high-school teachers within a radius of some 50 miles of the host institution.

This program is an experimental extension of the current programs of summer and academic-year institutes for high-school teachers sponsored by the National Science Foundation [*Science* **125**, 108 (18 Jan. 1957); 981 (17 May 1947)]. The high degree of teacher interest in such work is indicated by the fact that there were more than 25,000 applications for some 5000 openings in the 1957 summer and academic-year institute programs.

Bensley Memorial Fund

A memorial fund in honor of R. R. Bensley, formerly of the University of Chicago, is being established. The American Association of Anatomists will administer the fund, and the proceeds will be available equally to Canadians and citizens of the United States. Bensley made a number of classical contributions to cytology and to cytological chemistry. Contributions for this fund may be sent to Normand L. Hoerr, Western Reserve School of Medicine, Cleveland 6, Ohio.

Biochemistry at Brandeis

Brandeis University in Waltham, Mass., has established a graduate department of biochemistry as a result of a gift made to the university by the Dorothy H. and Lewis S. Rosenstiel Foundation. The initial staff appointments are as follows: Nathan O. Kaplan of the McCollum-Pratt Institute, Johns Hopkins University, professor and chairman of the department; and Martin D. Kamen of the department of radiobiology, Washington University Medical School, professor of biochemistry. Wil-

liam F. Loomis of the Loomis Laboratory will also have an appointment as professor of biochemistry. Assistant professors are Mary Ellen Jones of the Biochemical Research Laboratories at Massachusetts General Hospital, Lawrence Levine of the New York State Department of Laboratories, Lawrence Grossman of the National Institutes of Health, and William P. Jencks of the department of chemistry at Harvard University.

The department will offer a program of studies leading to the Ph.D. degree. An advanced training program for investigators with a Ph.D. or an M.D. degree is also planned. Research activities of the department will be carried out in a number of different areas, including intermediary metabolism in normal and tumor tissue, enzymology, immunochemistry, biochemical and immunogenetics, biochemical basis of chemotherapy, protein chemistry, plant and virus metabolism, radiobiology, problems in growth and differentiation, photobiology, microbial metabolism, and organic biochemistry. The department will begin its program on 1 July.

Hughes Department for Radiation Study

A new department of nuclear electronics has been announced by the Hughes Aircraft Company, Los Angeles, Calif. The department, headed by John W. Clark, will work with systems designers and manufacturers of components to measure radiation effects on materials and circuitry and to improve their performance under nuclear radiation conditions. The new group will specialize in radiation physics; dosimetry, particularly for high nuclear radiation rates; development of reliable techniques for radiation experiments, and design of radiation testing facilities.

AEC Radiation Protection Rule

The U.S. Atomic Energy Commission has amended its regulation on standards for protection of workers and the public against radiation to provide that those who are licensed shall promptly notify the commission of potentially serious accidents involving licensed material. They must now immediately notify the nearest AEC operations office of any incident involving licensed material which may have resulted in appreciable release of radioactive material or excessive exposure of individuals to radiation. This will enable the commission to assure that appropriate steps are taken to minimize the consequences of the incident, to determine its cause, and to initiate corrective action. Holders of licenses are required, also, to make a detailed report in writing, within 30 days, of all such incidents, regardless of their nature or extent, resulting in radiation exposures or concentrations of radioactive materials above permissible limits.

Spectrochimica Acta

Pergamon Press, Ltd., has announced that a reorganization of the scope of *Spectrochimica Acta* has been undertaken so as to take into account the changing emphasis in spectroscopy in recent years. The journal, which used to be mainly directed to problems of atomic emission spectroscopy and spectrographic analysis, will now reflect the impact upon chemistry, whether organic or physical, of molecular spectroscopy; problems of atomic emission spectroscopy will continue to be fully treated.

In the future, the journal will be published in four-issue volumes, containing the same number of pages as hitherto published in the six-issue volumes, and it is hoped that the journal will appear monthly. This increased rate of publication will make possible rapid publication of papers and also of short research notes, up-to-date reports on spectroscopic meetings, and general information of interest to spectroscopists. It is hoped that full-length papers can be published within 90 days of their acceptance and short communications within a maximum of 60 days.

Teacher Shortage in West Germany

The German Research Association, Bonn, has reported in its most recent survey that the shortage of science teachers in West German technical schools is "catastrophic." The report seems to indicate that some of the factors producing critical shortages in the United States are also operative in West Germany. These factors include an inadequate number of technical schools for the growing population, small teaching staffs, and poorly equipped technical schools.

The report says that there is a 60 percent shortage of engineers and assistants in the technical schools. The shortage of technical and workshop personnel in the school system has risen to 96 percent.

Further, the physical condition of the school buildings in many cases is very poor. Almost 50 percent of the schools specializing in chemistry were constructed before 1918. Between 20 and 30 percent of these institutions are described as "dilapidated." More than two-thirds of the schools are too small.

The income of science teachers compared with that of their graduates poses the same problem as in the United States. The shortage of technical personnel in engineering and chemical industries has also assumed a pattern similar to that in the United States. The Sunday editions of leading newspapers contain as many as eight and ten pages of classified advertisements for electronic, mechanical, construction, chemical, and steel engineers. Foreign concerns, including American organizations, have also been advertising for trained personnel to be employed in their German or overseas plants.

Public Relations and the Laboratory

Leland Haworth, director of Brookhaven National Laboratory, recently warned a group of Latin-American scientists that the public relations aspect of any atomic program is of primary importance. To demonstrate his point, he described the succession of events that followed the accident that took place at Brookhaven last month, when several laboratory staff members were injured, none fatally, in a chemical explosion.

Within minutes after the news of the explosion had been made public by bulletins and radio broadcasts, the laboratory switchboard was swamped. A Detroit editor had asked how much of Long Island had been destroyed; the *Times of London* wanted all details; one report said that there had been 1000 fatalities; the Oak Ridge National Laboratory wanted to known how it could help; and Haworth's daughter in California phoned that evening to see how he had come through the disaster.

Haworth deplored any unscheduled explosion, even in a test laboratory, but he emphasized that every nuclear research center should have well-organized public relations and press information sections fully prepared to deal with such emergencies. He went on to comment as follows about news and radio people: "They do things differently from scientists, who hold accuracy first and speed second. In some quarters, matters of public information are reversed. The Wednesday [explosion] event is a case in point. When word was passed out, there was a news chain reaction that went to many parts of the world."

N.Y.U.–Bell Laboratories Program

A graduate study center will be established by New York University at the Bell Telephone Laboratories this fall. At the center certain Bell Laboratories employees will be able to earn advanced engineering degrees by attending classes during regular business hours while receiving full-time pay.

A committee of Bell scientists worked

with the administration and faculty of the College of Engineering of New York University in drawing up a program selected from regular graduate offerings of the university. These courses, emphasizing particularly mathematics, physics, and basic communications, are designed to develop a strong background for engineers embarking on careers in creative work in the field of communications. This will be the first graduate center to be established by New York University in cooperation with industry.

Mental Health Awards

The Foundations' Fund for Research in Psychiatry has announced that *15 Oct.* is the next deadline for the submission of applications for research fellowships and research teaching grants in psychiatry, psychology, sociology, neurophysiology, and other sciences relevant to mental health. Interested persons and departments are invited to write for details to Foundations' Fund for Research in Psychiatry, 251 Edwards St., New Haven 11, Conn.

Zoological Nomenclature

The International Commission on Zoological Nomenclature has announced that beginning 6 Nov. it will start voting on the following cases involving the possible use of its plenary powers for the purposes specified. Full details were published in the 6 May issue of the *Bulletin of Zoological Nomenclature* (Vol. 13, Part 5): (i) *squilla Linnaeus*, 1758 (Cancer), suppression; *adspersus* Rathke, 1837 (*Palaemon*), designation of, as type species of *Palaemon* Weber, 1795 (Cl. Crustacea, Order Decapoda); (ii) *Dracunculus* Reichard, 1759, validation of, with *Gordius medinensis* Linnaeus, 1758, as type species (Cl. Nematoda); (iii) *Mansonia* Blanchard, 1901 (Cl. Insecta, Order Diptera), validation. Comments should be sent as soon as possible and in duplicate to the secretary of the commission, Francis Hemming, 28 Park Village East, Regent's Park, London, N.W.1.

Rare Chemicals

The following chemicals are wanted by the Registry of Rare Chemicals, Armour Research Foundation of Illinois Institute of Technology, 35 W. 33 St., Chicago 16, Ill.: alpha-Thujene; Trimethyl arsine; 2,4,6-Trimethylheptane; Perfluoroisovaleric acid; Perfluoro-n-heptane; Pentaiodobenzene; Pyrazinecarboxamide; 3,4-Lutidine; Sabinene; Santene; Tri-iso-butyl phosphate; Tri-n-hexyl phosphine oxide; 1,2,3,4-Tetraiodobenzene; 1,3,5-Triiodobenzene; 2,2′,4,4′-Tetramethyldiphenylamine; Potassium picrate; 1-Methylcyclohexanol; Ovalene; Isomenthone; Cadinene.

Proposed Legislation

Of the many bills introduced in Congress, some have a special relevance to science and education. A list of such bills introduced recently follows:

HR 6895. Discharge more effectively obligations of U.S. under certain conventions and protocols *re* institution of controls over manufacture of narcotic drugs. Karsten (D Mo.) House Ways and Means.

HR 6548. Amend Universal Military Training and Service Act, as amended, as regards persons in medical, dental and allied specialist categories. Vinson (D Ga.) House Armed Services.

HR 6719. Provide adjustments in organization and salary structure of Department of Medicine and Surgery in Veterans' Administration. Long (D La.) House Veterans' Affairs.

HR 6897. Provide that persons who have filed petitions for naturalization be employed as doctors in Medical Service of Department of Medicine and Surgery of Veterans' Administration. Knutson (D Minn.) House Veterans' Affairs.

HR 6126. Amend Civil Service Retirement Act to provide certain service in Coast and Geodetic Survey and Public Health Service be considered to be military service for purposes of such act. Broyhill (R Va.) (by request) House Post Office and Civil Service.

S 1862. Establish the Patent Office as an independent agency in executive branch of Government. O'Mahoney (D Wyo.), Wiley (R Wis.) Senate Government Operations.

HR 6602. Provide for establishment of a commission to study shortage of doctors of medicine in U.S. Dorn (R N.Y.) House Interstate and Foreign Commerce.

S 1863: Provide for limiting the life of a patent to a term commencing with date of application. O'Mahoney (D Wyo.), Wiley (R Wis.) Senate Judiciary.

S 1621. Amend act of Dec. 24, 1942 (56 Stat. 1086, 43 U.S.C., sec. 36b), entitled "An act to authorize Secretary of Interior to acquire lands or interest in lands for Geological Survey." Murray (D Mont.) Senate Interior and Insular Affairs.

HR 5817. Authorize for each fiscal year an appropriation into migratory bird conservation fund equal to all moneys received for Federal migratory-bird hunting stamps during next preceding calendar year. Dingell (D Mich.) House Merchant Marine and Fisheries.

HR 6541. Provide that Secretary of Commerce be authorized to furnish weather reports to air-pollution-control agencies. Roosevelt (D Calif.) House Interstate and Foreign Commerce.

S 1918. Amend P.L. 31, 84th Congress, 1st session, to increase authorization for appropriation to Atomic Energy Commission for construction of modern office building in or near D.C. to serve as its principal office. Pastore (D R.I.) Joint Committee on Atomic Energy.

H Con Res 163. Express sense of Congress that Atomic Energy Commission should establish an experimental nuclear reactor in state of Washington. Pelly (R Wash.) Joint Committee on Atomic Energy.

HR 5889. Authorize appropriations for Atomic Energy Commission for acquisition or condemnation of real property or any facilities, or for plant or facility acquisition, construction or expansion. Durham (D N.C.) Joint Committee on Atomic Energy.

HR 5954. Provide for an experimental research program in cloud modification. Baring (D Nev.) House Interstate and Foreign Commerce.

HR 6005. Make evaluation of recreational benefits and wildlife development resulting from construction of any flood control, navigation, or reclamation project an integral part of project planning. Trimble (D Ark.) House Interior and Insular Affairs.

HR 6571. Provide for establishment of a Federal Nuclear Science Academy. Patterson (R Conn.) Joint Committee on Atomic Energy.

HR 6691. Authorize a 10-year program for acquiring national migratory bird refuges and areas. Reuss (D Wis.) House Merchant Marine and Fisheries.

HR 6807. Provide for establishment of a fish hatchery in state of Wisconsin. Withrow (R Wis.) House Merchant Marine and Fisheries.

HR 6959. Authorize Secretary of Interior to cooperate with Federal and non-Federal agencies in augmentation of natural food supplies for migratory water-fowl. Boykin (D Ala.) House Merchant Marine and Fisheries.

HR 5877. Amend Internal Revenue Code of 1954 to allow additional income tax exemption for dependent who is student. Jennings (D Va.) House Ways and Means.

HR 6105. Amend Internal Revenue Code of 1954 to allow deductions for amounts paid by teachers for further education. Teague (R Calif.) House Ways and Means.

Scientists in the News

EDWIN C. KEMBLE, director of the Institute for Teachers of Science and Mathematics which Harvard University will conduct during the coming aca-

demic year, will become professor emeritus on 1 July. Kemble, a theoretical physicist with long experience in teaching elementary and advanced scientific courses, has been closely identified with Harvard's general education program in physical science since its inception. At present he is preparing *An Introduction to Physical Science,* a textbook for the use of general education students. He will devote full time next year to the new institute for high-school teachers, which is part of a program being sponsored by the National Science Foundation.

Kemble was chairman of the department of physics at Harvard from 1940 to 1945 and in charge of the instruction in physics for the Army and Navy officer-candidate training units at the university during World War II. During the same period he was engaged in propeller research for the Navy at the Underwater Sound Laboratory. In the spring of 1945 he was sent overseas as deputy scientific chief of the ALSOS military intelligence mission.

He attended Ohio Wesleyan University and Case Institute of Technology. He received his B.S. degree in 1911 from Case, which bestowed an honorary doctorate in 1931. He received his A.M. degree at Harvard in 1914, and his Ph.D. degree in 1917.

His first teaching experience was at Carnegie Institute of Technology in 1911–13; in 1917 and 1918 he was employed as an engineering physicist by the Curtis Aeroplane Company at Buffalo, N.Y.; and in 1919 he returned to Harvard as instructor in physics. He has been a professor since 1930, the year in which he also earned a Guggenheim fellowship.

Most of Kemble's research activity has been in theoretical atomic physics, including band spectra, statistical mechanics, and the philosophic problems of quantum mechanics. As chairman of the National Research Council Committee on Radiation in Gases, he was coauthor of the committee's report *Molecular Spectra in Gases,* published in 1937. That same year he also published *Fundamental Principles of Quantum Mechanics.* He was chairman of the Coulomb's Law Committee of the American Association of Physics Teachers, 1946–49, and chairman of the physics section of the National Academy of Sciences, 1945–48. He is a member of the National Academy of Sciences and a fellow of the American Physical Society and the American Academy of Arts and Sciences.

ALLISON BUTTS, professor of metallurgy at Lehigh University, who has been teaching at that institution for the past 41 years, was recently honored at the tenth annual faculty dinner. He will retire on 30 June.

Technical editor and author as well as teacher, Butts served as head of Lehigh's department of metallurgy from 1952 until last year, when he gave up administrative duties to devote full time to teaching, research, and writing. Prior to joining the Lehigh faculty in 1916, he was a research chemist for the United States Metals Refinery Company, Carteret, N.J.

He has served as associate editor of *The Mineral Industry* for 11 years and as consultant and contributor to several dictionaries and encyclopedias. He is the author and editor of a number of books. His latest volume, for which he was editor, is *Copper: the Science and Technology of the Metal, Its Alloys, and Compounds.*

Butts was graduated from Princeton University with a bachelor of arts degree. He received his bachelor of science degree from the Massachusetts Institute of Technology.

Sir JOHN COCKROFT, director of the British Atomic Energy Research Establishment, left on 17 May for a lecture tour in Poland as a guest of the Polish Academy of Science.

A. J. P. MARTIN, winner of the Nobel prize in chemistry, and his colleague A. T. JAMES came to the United States recently to receive the annual special award of the Society of Cosmetic Chemists. The two British scientists were honored for their publications on gas-liquid chromatography.

CARL G. PAULSEN, chief hydraulic engineer for the U.S. Geological Survey, has retired and LUNA B. LEOPOLD has been promoted to succeed him. Also, RAYMOND L. NACE has been advanced to assistant chief of the Survey's Water Resources Division.

Paulsen had been chief of the Water Resources Division for more than a decade. With more than 45 years of Government service already behind him, he will continue to serve as Delaware River Master and will continue also in a special advisory capacity on a number of international water commissions.

Paulsen entered Government service in 1911 as hydrographer with the Bureau of Reclamation. He earned the bachelor of science degree in civil engineering from the University of Idaho in 1913, and joined the Geological Survey in the same year. He became chief of the surface water branch in 1931, assistant chief hydraulic engineer in 1940, and chief in 1946.

In addition to service in the United States, Paulson has had general supervision of hydrologic investigations in Alaska and Hawaii and has undertaken similar work in Iraq. He is also a member of several joint international engineering boards for the International Joint Commission between Canada and the United States.

WARREN S. WOOSTER, assistant research oceanographer at the University of California's Scripps Institution of Oceanography, will start a 1-year leave of absence on 15 June to direct the marine research program of the Republic of Peru. He will be stationed in Lima.

Wooster's appointment stems from a recent agreement between the Peruvian Council of Hydrobiological Investigations, the Scripps Institution, and the Inter-American Tropical Tuna Commission. Under the agreement, the Scripps Institution will train Peruvian oceanographers and will give leave of absence to staff members chosen to aid the Peruvian research studies. In return, the institution will receive data collected in Peruvian waters.

The Peruvian council is supported by four groups: the Peruvian Navy; the Guano Company, which harvests the fertilizer deposits left by sea birds on the rocky islands off the Peruvian coast; the Peruvian Fish and Wildlife Service; and the Peruvian fishing industry. Financial support for the marine research program comes from fees paid by American tuna fishermen, who pay to collect bait in Peruvian waters and to use Peruvian ports.

Wooster's task will be to organize and direct the new research program. His first project will be an oceanographic study of the northern boundary of the Peru Current, where most of the tuna fishing is done. He will also study "El Niño," a warm current from the north which occasionally sweeps down the Peruvian coast and causes the death of many fish and birds.

Y. C. LEE has been named director of research and planning for the Liquid Engine Division of the Aerojet-General Corporation, Azusa, Calif. Lee, a native of China who served with the Chinese Air Force from 1931 to 1935, was graduated from the California Institute of Technology with a B.S. in aeronautical engineering in 1938 and joined Aerojet-General in 1949.

The following men received awards during the recent annual meeting of the Aero Medical Association:

Col. JOHN P. STAPP, USAF (MC), chief, Aero Medical Field Laboratory, Holloman Air Force Base, N.M., is the first recipient of the Eric Liljencrantz award, established by Pfizer Laboratories, division of Chas. Pfizer & Co., Inc. The award, consisting of a plaque and an honorarium, will be given annually for outstanding achievement in the solution of problems of high-speed flight and ac-

celeration. The late Dr. Liljencrantz, whose memory the award perpetuates, was a reserve naval Medical Corps officer who lost his life in an aircraft accident in 1942 while conducting experiments with a new type of accelerometer.

Maj. DAVID G. SIMONS, USAF (MC), chief, space biology branch, Aero Medical Field Laboratory, Holloman Air Force Base, N.M., received the Arnold D. Tuttle award for the best research report published in the *Journal of Aviation Medicine* in the past 2 years. The winning article was "1954 Aero medical field laboratory balloon flights; physiological and radiological aspects."

Capt. CHARLES F. GELL, MC, USN, director, Air Crew Equipment Laboratory, Naval Material Center, Philadelphia, received the Theodore C. Lyster award, which is given annually for outstanding achievement in the general field of aviation medicine. Gell is a specialist in acceleration.

Brig. Gen. EUGEN G. REINARTZ, USAF (MC), retired, Carmel Valley, Calif., received the Raymond F. Longacre award, which is given annually for outstanding accomplishments in the psychologic and psychiatric aspects of aviation medicine.

ROBERT P. RICE, formerly chief chemist at the Columbia Southern Chemical Corporation, Jersey City, N.J., has joined the American Potash and Chemical Corporation as chief control chemist at the company's Henderson, Nev., plant.

HENRY KOFFLER, professor of bacteriology at Purdue University, received the $1000 Eli Lilly research award in bacteriology and immunology during the recent meeting of the Society of American Bacteriologists. He was honored for research achievements that include: discovery of unique chemical structures that permit some organisms to thrive at temperatures high enough to kill most living creatures; studies on structural polymers in microorganisms, especially fibrous proteins in bacteria and cell-wall substances in fungi; clarification of the intimate details of metabolism in such molds as those that synthesize penicillin and streptomycin; and development of the peptide antibiotic circulin (including its crystallization and studies on its chemistry), and the demonstration that this antibiotic acts on the surface structures of bacterial cells rather than within the cells.

R. W. TOWNLEY, chemist, who has headed basic research at Personal Products, Milltown, N.J., for the past 3 years, resigned recently to form his own firm, known as Townley Research and Consulting, Gillette, N.J.

NATHAN J. SMITH, associate professor of pediatrics at the University of California, Los Angeles, has been named chairman of the University of Wisconsin Medical School's department of pediatrics, pediatrician-in-chief of University Hospitals, and the university's first Dr. Alfred D. Daniels professor on diseases of children.

Also at Wisconsin, JOSHUA LEDERBERG has been named half-time chairman of the department of medical genetics. Lederberg will continue his work, on a half-time basis, in the department of genetics of the College of Agriculture.

The following men were honored at the first Pan American Cancer Cytology Congress: JOSE M. MEZZADRA of the University of Buenos Aires, Argentina, received the University of Miami award of merit; GEORGE GEY of Johns Hopkins University received the Wien award for 1956; and WILLIAM TERZANO of Buenos Aires, Argentina, received the Wien award for 1957.

EDWARD L. MICHAELS, specialist in electronics and color television, will teach electrical engineering classes at the Finland Institute of Technology, Helsinki, during a leave of absence from the Hughes Aircraft Company research laboratories.

FERDINAND P. BEER, who joined the Lehigh University faculty in 1947, has been named head of the department of mechanics. The establishment of a curriculum in engineering mechanics starting this September was approved by the university's board of trustees at its spring meeting.

C. D. DAVIS of the University of Missouri School of Medicine has resigned as professor in obstetrics and gynecology to accept an appointment to Yale University Medical School. Also at Missouri, W. A. SODEMAN has resigned as chairman of the department of medicine effective 1 Aug.

HOMER R. WOLFE has joined the staff of the Wenatchee (Wash.) Field Station of the U.S. Public Health Service's Communicable Disease Center. As an entomologist he will be conducting exposure studies to evaluate the health hazards associated with the agricultural uses of pesticides. Wolfe leaves the Tree Fruit Experiment Station of the State College of Washington, where he has been employed as an entomologist for the last 10 years. He replaces GORDON S. BATCHELOR, who resigned in November 1956 to do technical service work for the General Chemicals Division of the Allied Chemical and Dye Corporation.

D. T. SMITH, James B. Duke professor of bacteriology in the Duke University Medical School and chairman of the department of microbiology and the department of preventive medicine and public health, has received the Trudeau medal of the National Tuberculosis Association. He was selected for the award as the person who has made the most outstanding contribution in tuberculosis work in the United States.

Dartmouth College has announced that the following professors will retire this year: FREDERICK PAGE and JAMES POOLE, botany; ANDREW SCARLETT, chemistry; and ELLSWORTH D. ELSTON, geology.

Recent Deaths

NELL V. BEEBY, Jackson Heights, N.Y.; 60; executive editor of the American Journal of Nursing Company; 17 May.

ARTHUR F. BENTLEY, Paoli, Ind.; 86; author, philosopher, and political scientist whose writings included works on mathematics and the philosophy of science; 21 May.

KARL F. BONHOEFFER, Goettingen, Germany; 58; head of the Max Planck Institute for Physical Chemistry; announced 20 May.

DOUGLASS BURNETT, Baltimore, Md.; 85; utilities executive, early research worker in the development of electricity who was associated with Thomas A. Edison; 16 May.

THÉOPHILE DE DONDER, Brussels, Belgium; 84; professor emeritus of mathematical physics at the University of Brussels; 11 May.

FLOYD C. FAIRBANKS, Kingsville, Tenn.; 75; retired professor of physics and astronomy at the University of Rochester; 22 May.

WALTER M. LIPPINCOTT, Lynbrook, N.Y.; 85; retired orthopedic surgeon and former professor at New York Post-Graduate Hospital and Medical School; 15 May.

HAROLD L. LYON, Honolulu, Hawaii; 77; director emeritus of the Experiment Station, Hawaiian Sugar Planters' Association; botanist and former director of the Foster Botanical Gardens; 15 May.

WERNER WOLFF, Annandale, N.Y.; 53; professor of psychology and chairman of the department at Bard College; 18 May.

Erratum: In "Potentially simple technique for rearing "germ-free fish" by Evelyn Shaw [*Science* 125, 987 (17 May 1957)] the second sentence of the second paragraph should read: "Of 25 trials (consisting of 10 eggs per trial) treated in this manner (3), eight trials remained germ-free throughout the experiment."

Reports

Enhancement of Activity of Nerves by X-rays

No report of the response of excised mammalian nerves during x-irradiation has heretofore been published (*1*). Recordings made at the end of irradiation or at considerable periods after irradiation fail to show the dynamic changes that take place during irradiation which are reported in this paper (*2*). Nerves transferred from irradiation chambers to recording chambers have failed to give the highly reproducible values that are necessary in quantitative work of this type.

The paired ventral caudal nerves of the rat were chosen because they possess a uniform fiber spectrum (*3*) and therefore exhibit sharp, compact spike potentials. They are long nerves with a minimum of branching, well adapted to studies on conduction velocity. Their activity is not highly dependent on temperature.

Each nerve was irradiated on platinum electrodes in a specially constructed, sealed chamber, which was affixed to the x-ray tube. A fine spray of oxygenated Ringer-Locke's solution was capable of keeping the nerve in excellent condition for periods well over 24 hours, with adequate provision to keep the electrodes from shorting out. The stock of solution which served as the source of the fine spray was itself not irradiated.

X-irradiation was carried out at 280 kv (peak) and 20 ma at a dose rate of 6 kr/min. Electrophysiological apparatus was employed to procure records of the response of the nerve to square-wave stimulation during irradiation. Single supramaximal stimuli were applied only at the time a recording was made. Simultaneous recordings from two pairs of electrodes, one near the proximal end of the nerve, the other near the distal end of the nerve, separated by 50 mm, were displayed on the face of a cathode-ray tube. Photographic records of the responses of the nerves were made from these tracings; they were later projected on a screen for exact determination of values. The amplitude of spike potential and the conduction velocity were established for control nerves and for nerves under irradiation.

Irradiation was begun only after a period of stabilization during which the output of the nerve was shown to be constant for a period of time exceeding that of the period of irradiation. Figure 1 shows the result of x-irradiation on the spike amplitude and conduction velocity of a typical nerve. An almost immediate response to x-irradiation is obvious in Fig. 1, but it was not anticipated that the effect would be to enhance the activity of the nerve. There was an initial small increase in conduction velocity followed by a steady decrease which was quite independent of the increase in spike amplitude. The increase in spike amplitude, which has now been recorded in more than 50 cases, has been as great as 60 percent, with a mean of 25.6 percent; in only 6 percent of the cases did the nerve fail to show an increase in spike amplitude as a result of irradiation. Conduction velocity, on the other hand, has shown an average increase of only 5.8 percent, with 20 percent of the nerves failing to show an increase. In one sense, the conduction velocity was more sensitive to x-rays than the spike amplitude, for it began to decrease long before the spike amplitude began to decrease; in another sense, it was less sensitive, for the response was less and, at expiration of the nerve, when spike amplitude was essentially zero, conduction velocity was still approximately 50 percent of the original velocity.

Factors that affect the ability of the nerve to respond as a result of x-irradiation are under extensive investigation. It may be noted that the increase in spike amplitude is greatest for nerves that are kept in the solution the shortest time prior to irradiation. After 24 hours, the increase in spike amplitude, in response to x-irradiation, is less than 5 percent. A second factor of importance in the magnitude of the response of the nerve to x-irradiation is the dose rate. At higher dose rates, the increase in spike amplitude is considerably less than it is at lower dose rates. This suggests that there may be two competing processes proceeding at different rates. One tends to increase the output of the nerve, and the other tends to destroy the activity of the nerve. It is the latter that is observed in most biological responses to x-irradiation.

The increased output of the nerve is not a reversible phenomenon, but is the result of an altered condition of the nerve, possibly an alteration in the permeability of the membrane, and is not dependent on concomitant bombardment by x-rays. This was proved by the fact that nerves continued to respond at high levels when, during the course of irradiation, the x-ray beam was turned off.

An explanation of the increase in output of the nerve under irradiation may be sought in the fact that x-irradiation may increase the ionic permeability of the membrane, which, in turn, may increase the magnitude of the action potential. After the increase in permeability which is manifested by an increase in the action potential, further increase in permeability, to the point of impairment of the activity of the nerve, would then lead to a decline in activity and ultimate

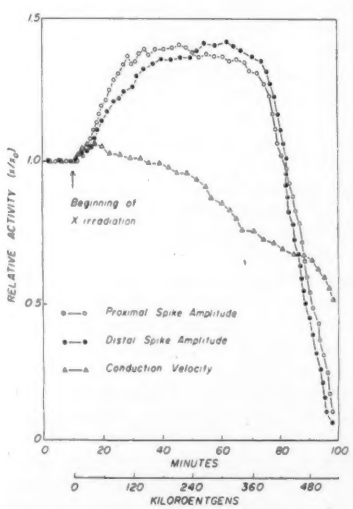

Fig. 1. Relative activity of caudal nerve of a rat as a function of time and dose of x-rays. Two pairs of electrodes were utilized to give the values. One pair was located proximally and the other distally, separated by 50 mm. The value of proximal spike amplitude, distal spike amplitude, or conduction velocity at time t is represented by x, while the corresponding value at the beginning of irradiation is represented by x_0.

All technical papers and comments on them are published in this section. Manuscripts should be typed double-spaced and be submitted in duplicate. In length, they should be limited to the equivalent of 1200 words; this includes the space occupied by illustrative or tabular material, references and notes, and the author(s)' name(s) and affiliation(s). Illustrative material should be limited to one table or one figure. All explanatory notes, including acknowledgments and authorization for publication, and literature references are to be numbered consecutively, keyed into the text proper, and placed at the end of the article under the heading "References and Notes." For fuller details see "Suggestions to Contributors" in *Science* 125, 16 (4 Jan. 1957).

extinction. A sound foundation for this hypothesis is given by the work of Rothenberg (*4*), who showed that x-irradiation increased the permeability of the squid axon to sodium-24; the importance of Na^+ ions in the propagation of the nerve impulse is well known. The problem still to be answered, however, is why the conduction velocity falls during irradiation while the spike amplitude is rising.

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References and Notes

1. This report is based on a paper read at the first National Biophysics Conference at Columbus, Ohio, 4 Mar. 1957.
2. This research was performed under contract No. AT(11-1)-205 between the U.S. Atomic Energy Commission and the University of Notre Dame.
3. P. O. Chatfield and C. P. Lyman, *Am. J. Physiol.* 177, 183 (1954).
4. M. A. Rothenberg, *Biochim. et Biophys. Acta* 4, 96 (1950).

15 March 1957

Mode of Action of Antigen and Other Smooth-Muscle Stimulants

Smooth muscle from an antigenically sensitized animal contracts upon reexposure *in vitro* to the antigen (*1*). This phenomenon, the Schultz-Dale reaction, may form a basis for several hypersensitive conditions (reviewed by Seegal, *2*). Because the Schultz-Dale reaction is prevented by botulinum toxin, and by certain substances that are capable of interfering with conduction in nerve, involvement of nerve in the process seems likely (*3*). Ganglionic blocking agents do not prevent the reaction. This report (*4*) offers information concerning the relationship of the Schultz-Dale reaction to the action of other smooth-muscle stimulants.

Ileum from guinea pigs sensitized to egg albumin was set up in a muscle bath containing Tyrode's solution and arranged for kymographic recording of the contractions of the longitudinal muscle as previously described (*3*). Supposed inhibitors and stimulants were added to the bath. The concentration of antigen chosen was 10 times that which produces a just-perceptible contraction of the ileum. Concentrations of the other stimulants were as follows: serotonin, 2.0 μg/ml; nicotine, 2.0 μg/ml; acetylcholine, 0.02 μg/ml; barium chloride, 0.2 mg/ml; and histamine, 2.0 μg/ml. Several concentrations of each inhibitor were used; the concentrations given in subsequent paragraphs are those that illustrate most clearly the difference between the actions of the various stimulants.

Our present interpretation of the results is given in terms of a diagram (Fig. 1), patterned after one of Ambache (*5*), which attempts to indicate mechanisms consistent both with our data and with much of the enormous pertinent literature. Solid arrows indicate hypothetical pathways of stimulation, and dashed lines indicate points at which inhibition is believed to take place. The principal steps in the development of the relationships thus expressed follow:

Contraction of muscle owing to antigen, to serotonin, or to nicotine is prevented by low concentrations of alcohols and urethanes. This suggests a common step in the mechanisms of the actions of these three stimulants, probably conduction in nerve, since alcohols and urethanes block conduction in the concentrations that were used (*6*).

Stimulation by antigen and by serotonin (but not by acetylcholine, histamine, or barium chloride) is prevented by structural analogs of serotonin, such as gramine, yohimbine, and bufotenine (all 0.02 mg/ml). This suggests that antigen may act by liberating serotonin, as Fink (*7*) has concluded from studies with mouse uterus.

Stimulation by antigen is blocked by botulinum toxin, but stimulation by serotonin is not so blocked (*3*). This suggests that liberation of serotonin by antigen is the process blocked by botulinum toxin.

The mechanism of stimulation by nicotine seems to be more complex, since ganglionic blocking agents are capable of inhibiting, often without completely abolishing, the response to this substance (*5, 8*). Moreover, nicotine stimulation is abolished by butolinum toxin (*9*). Nicotine stimulation was also found to be prevented by the structural analogs of serotonin, so nicotine may also act by liberating serotonin.

Lower alcohols (ethyl, 1.0 percent; propyl, 1.0 percent; butyl, 0.4 percent; and amyl, 0.2 percent) do not prevent the contraction of muscle owing to acetylcholine or histamine, whereas higher alcohols (hexyl, 0.04 percent; heptyl, 0.02 percent; and octyl, 0.02 percent) prevent stimulation by acetylcholine but not by histamine. Thus, histamine seems to act at a site closer to the contractile mechanism than does externally applied acetylcholine. This observation recalls the demonstration by Dale and Gaddum (*10*) that the site of action of externally applied acetylcholine is probably not identical with that of the acetylcholine liberated by cholinergic nerve endings. The data also confirm results of others (*9, 11*) that suggest that the site of action of barium chloride, often supposed to be a direct muscle stimulant, may be close to that of acetylcholine.

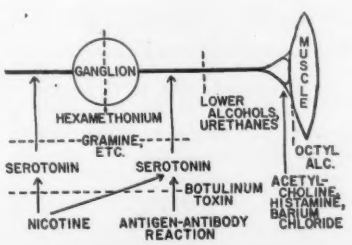

Fig. 1. Hypothetical sites of action of stimulants and inhibitors upon smooth muscle and the associated nerve structures.

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28 February 1957

Instrumental Artifacts in the Determination of Difference Spectra

A. H. Mehler (*1*) has warned of the serious errors that may arise because of the unavoidable stray light within the monochromator of single-beam spectrophotometers when a photomultiplier detector is employed to measure the difference in optical density of two solutions of relatively high absorbance. This was illustrated by the apparent deviation from Beer's law when the absorbance of a constant amount of each of various materials was determined as the difference between two solutions of increasing absolute concentration.

This report seeks to extend this warning to the practice of determining the absorption characteristics of a given compound in the presence of other absorbing species by using an appropriate blank to "zero out" the absorption owing to the extraneous compounds and thus to obtain a "difference spectrum." We have

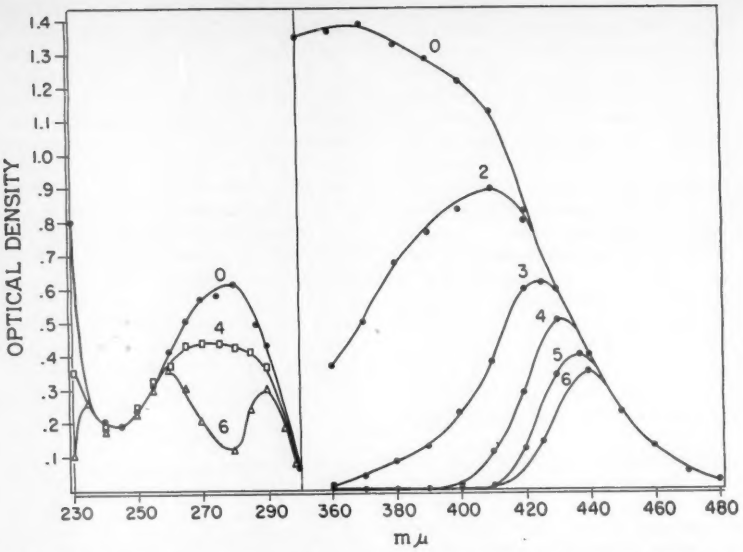

Fig. 1. Difference absorption spectra of tryptophan and 2,4-dinitrophenol, obtained with Beckman DU spectrophotometer and photomultiplier. (Left) Tryptophan. Each curve represents the difference spectrum due to $1 \times 10^{-4}M$ tryptophan in 0.05M phosphate, pH 7.9, and 0.005 percent Versene obtained as the difference between 0 and $1 \times 10^{-4}M$ (●), 4 and $5 \times 10^{-4}M$ (□), and 5 and $6 \times 10^{-4}M$ (△) respectively. (Right) 2,4-Dinitrophenol. Each curve represents the difference spectrum due to $1 \times 10^{-4}M$ dinitrophenol in 0.05M phosphate, pH 7.8, obtained as the difference between 0 and $1 \times 10^{-4}M$, 1 and $2 \times 10^{-4}M$, 2 and $3 \times 10^{-4}M$, and so forth. The indicated figure represents the lower concentration.

observed that, with solutions of only moderately high absorbance, such difference spectra may be seriously misleading.

Buffered solutions of 2,4-dinitrophenol and of tryptophan were prepared whose concentrations were $1 \times 10^{-4}M$, $2 \times 10^{-4}M$, $3 \times 10^{-4}M$, and so forth. Difference spectra were determined between succeeding pairs in the series so that in each case the absorption spectrum due to a $1 \times 10^{-4}M$ solution was obtained. The results are shown in Fig. 1.

It is clear that the nature of the *apparent* difference absorption spectrum changes as the absolute concentration of the absorbing material increases. The deviations from the true absorption spectra of these compounds are due entirely to the stray polychromatic light within the monochromator, which causes the apparent difference in optical density due to a given level of absorbing compound to decrease progressively as the absolute concentration increases. The use of a photomultiplier detector that permits determination of difference spectra between solutions of high absolute absorbance increases the likelihood of this instrumental artifact. Since this effect is most pronounced at the absorption maxima and is of least significance at the absorption minima, the entirely misleading data of Fig. 1 result. If these were difference spectra that had been obtained with a view toward identifying an unknown compound, they would be unrecognizable. In consequence, only in double-beam optical systems where the stray light is negligible may difference spectra obtained at high absolute absorbances be determined with confidence (*2*).

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2. These observations were made in the course of studies variously supported by the National Institutes of Health, the U.S. Atomic Energy Commission, and the National Science Foundation.

12 March 1957

Photosensitive Pigments from Retinas of Deep-Sea Fishes

In November 1956, a new group of visual pigments was described briefly by Denton and Warren (*1*) from several species of deep-sea fishes. The new pigments were named "chrysopsins" or visual golds and characterized as having maximum sensitivity to light at a wavelength about 20 mμ less than the $\lambda_{max.}$ of rhodopsin. The chrysopsins were not extracted from the retina, but were demonstrated by determining the density changes when fresh retinas were bleached with white light.

Through the kindness of Carl L. Hubbs of the Scripps Institution of Oceanography, bathypelagic deep-sea fishes were collected on an expedition made by the Scripps vessel *Paolina-T* in February 1957. The fishes were caught at night with a midwater trawl at depths of 280 to 380 fathoms near Guadalupe Island, Baja California, Mexico. Hubbs generously sorted the trawl collections and made field identifications by dim red light (*2*). The retinas were removed, and digitonin extracts were prepared by standard methods (*3*). Spectrophotometric examination and bleaching with narrow-band colored light allowed analysis of the retinal pigments present in these extracts (*4*).

In general, the results of Denton and Warren were confirmed, $\lambda_{max.}$ of the photosensitive pigment of *Argyropelecus affinis* Garman being 478 mμ (Fig. 1). The pigment was demonstrated to be homogeneous by partial bleaching experiments (*3*). The absorption spectrum and the hydroxylamine difference spectrum of this retinal extract were in good agreement with the theoretical curve constructed from Dartnall's nomogram (*5*) for a visual pigment with $\lambda_{max.}$ of 478 mμ. The greater absorption of the extract (curve 1) in the short-wavelength portion was caused by the presence of light-absorbing impurities. The difference spectrum (curve 3) falls below the theoretical curve in this region because of the appearance of the violet-absorbing product of bleaching. The absorption of the product of bleaching was maximal at 375 to 380 mμ (pH 8.3) and at 365 to 370 mμ when hydroxylamine was added, indicating that retinene$_1$ was the chromophore of the light-sensitive pigment (*6*). This pigment is therefore provisionally called pigment 478$_1$ (the subscript means that retinene$_1$ is the chromophore).

A retinal extract of *Sternoptyx obscura* Garman of the same family, Sternoptychidae, had a different photosensitive pigment with $\lambda_{max.}$ at 485 mμ, but with the same product of bleaching. In the unrelated *Bathylagus wesethi* Bolin (family Argentinidae), however, a 478$_1$ pigment like that of *Argyropelecus* was mixed in the extract with a rhodopsin ($\lambda_{max.}$ = 500 mμ) in the ratio of about 4/1. This was determined by selectively bleaching the red-sensitive rhodopsin with red light and then bleaching the 478$_1$ pigment with orange and yellow light. The products of bleaching of the two pigments were spectrally identical, suggesting that retinene$_1$ was the chromophore of each.

Further indications of diversity were found in extracts of other deep-sea fishes, each of which had only a single

photosensitive pigment with the same product of bleaching as *Argyropelecus* and *Bathylagus*. *Stomias atriventer* Garman (family Stomiatidae) and the unrelated *Lampanyctus mexicanus* Gilbert (family Myctophidae) both had 490_1 pigments. Slightly different was an extract of *Melamphaes bispinosus* Gilbert (family Melamphaidae) with a light-sensitive 488_1 pigment.

All the extracts showed surprisingly high concentrations of the photosensitive pigments. (In Fig. 1, curve 1, the optical density at 475 mμ was 0.562 in an extract made from two small eyes.) The fishes examined probably all have pure-rod retinas. With histological methods, Brauer (*7*) studied species of each genus reported here and found only rods in each of them. There is no direct evidence that the light-sensitive retinal pigments of these deep-sea fishes are visual pigments. This seems probable, however, in view of their characteristic shape, which agrees with Dartnall's nomogram, and their products of bleaching, which are indicative of retinene$_1$. Although the tendency of the retinal pigments to be shifted toward the blue end of the spectrum was common to all the deep-sea fishes studied, there is no systematic trend apparent from this preliminary survey. The extracted pigments differ from rhodopsins in their $\lambda_{max.}$ but not in their retinene. Their wavelengths of maximum absorption approach the photosensitive pigments of certain mammals which also have $\lambda_{max.}$ less than 500 mμ (*8*). Because of this continuous spread of retinene$_1$ pigments, the use of the term *chrysopsin* is confusing and therefore is not followed. The presence of a dual, light-sensitive pigment system in a pure-rod eye (*Bathylagus*), based on the single carotenoid retinene$_1$, is particularly interesting (*9*).

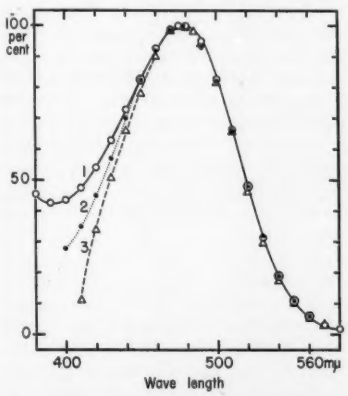

Fig. 1. Photosensitive pigment of *Argyropelecus affinis*. Curve 1, absorption spectrum of unbleached retinal extract (no significant absorption between 580 and 700 mμ); curve 2, constructed from Dartnall's nomogram, assuming a maximum at 478 mμ; curve 3, hydroxylamine experiment, difference spectrum (maximum change, 0.071 optical density units) after exposure of extract to yellow light (580 mμ).

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2. I am indebted to Alfred W. Ebeling, also of Scripps Institution of Oceanography, who determined the six species of fishes studied.
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9. A detailed account of this investigation is in preparation.

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21 March 1957

Factors Affecting the Appearance of Picture Varnish

Among the factors that affect the appearance of a picture varnish of the spirit type, one might consider that the refractive index of the resin would play a major role. Refractive index has entered the literature regarding picture varnishes, yet I do not recall that its role has ever been demonstrated. There has certainly not been sufficient discussion of the subject to reach agreement on whether the refractive index should be low (*1*) or similar to that of aged linseed oil (linoxyn) (*2*). In seeking to develop new protective coatings for the artist and conservator, our laboratory gave consideration to this problem. This report presents reasons for believing that variations in the refractive index of the resin, within the range 1.43 to 1.54, play a relatively minor, if not negligible, role in determining the appearance of spirit varnishes on the surface of paintings. Particular attention is drawn to variations in appearance that are attributable to differences in the viscosity grades of the resin.

Fresnel's law relates the intensity of reflected light in terms of the angle of incidence and the refractive index. Under the restricted condition of perpendicular incidence, the Fresnel equation may be simplified to

$$I = \left(\frac{n-1}{n+1}\right)^2$$

where I is the intensity of light of unit amplitude which is reflected and n is the refractive index. With this equation, values as follows may be calculated: $n = 1.1$, 0.23 percent reflection; 1.3, 1.7 percent; 1.5, 4.0 percent; 1.7, 6.7 percent. These values are essentially those attained at angles of incidence up to about 40 deg.

The range of refractive indices in organic coatings applied in the conservation of art objects is limited and is perhaps no more than 0.17. Limitation is understandable if only atoms of carbon, hydrogen, and oxygen are to be used in building the molecules of durable thermoplastics. By calculations from the simplified Fresnel equation, it is estimated that a linoxyn film of refractive index 1.57 (near the upper limit) would reflect 4.9 percent of the incident light. A film of refractive index 1.467 (near the lower limit) would reflect 3.6 percent. If reflection at the varnish-oil interface is considered, application of a varnish of refractive index 1.57 would result in no reflection and application of one of refractive index 1.467 would result in less than 1-percent reflection.

Frequently, then, in picture varnish, we are concerned with absolute differences in reflection of no more than 1 or 2 percent. This is close to the limit of the sensitivity of the eye. Over a wide range of intensities, the relative threshold of just-perceptible-brightness is about 1 percent of the intensity level to which the eye is adjusted (*3*).

Regardless of the proportion of incident light which is reflected, one's impression of a surface is strongly influenced by the relative sharpness or diffuseness of the reflected light. Methods of expressing the distribution of the reflected light are aspects of "gloss" or "glossiness." Judd (*4*) lists five types, five ways of expressing gloss: specular gloss, contrast gloss, distinctness-of-image gloss, sheen, and bloom.

If one observes only the reflected light, the relative change from 3.6 to 4.9 percent is considerable. However, in viewing a painting, the eye is perhaps adjusted to the general level of illumination in the room. An absolute difference of 1 to 2 percent is frequently negligible in comparison with variations in diffuse reflection—that is, gloss. In their investigation of ceramic glazes, Dinsdale and Malkin (*5*) found that the measured and observed gloss did not follow in the order of increasing refractive index from 1.51 to 1.66.

Even with porous paint, experiment has demonstrated that the fluidity of a varnish at a given concentration of resin can play a greater role than refractive index in determining appearance. A lean paint of Bakelite polyvinyl acetate AYAT and ultramarine was prepared. The

Table 1. Color of lean polyvinyl acetate-ultramarine paint when varnished.

Varnish resin	Solvent	Color	Viscosity grade (centipoise)	Refractive index of resin
Experimental polymethacrylate	Cycloparaffins	Light	22	1.48
Experimental polymethacrylate	Cycloparaffins	Dark	8	1.48
AW-2	Cycloparaffins	Dark	1.2	1.52
Dammar	Turpentine	Dark	1.3	1.53
Bakelite polyvinyl acetate AYAB	Toluene	Dark	9	1.467
Bakelite polyvinyl acetate AYAT	Toluene	Light	114	1.467
Polyvinyl alcohol	Water	Light	~400*	1.51

* Value determined in water.

paint did not rub off when it was rubbed with the hand, and yet it was porous to the applied varnishes. When the coat of varnish had dried, the value of the blue was noted simply as "dark" or "light." Table 1 shows that varnishes prepared with resins of high viscosity grade apparently do not form an intimate contact with the paint, with the result that the color appears light irrespective of the refractive index. Practical applications immediately come to mind when one does not wish to darken colors in pastels and porous paints.

The truly outstanding difference between the properties of the traditional picture varnishes, dammar and mastic, and those of many proprietary polymers is not in their refractive indices, but in the viscosity of their solutions. In place of intrinsic viscosity, we have used the viscosity at 20 percent solids by weight in toluene at 70°F as a convenient measure to characterize resins, giving it the name "viscosity grade." A similar measurement has been used to classify chlorinated rubber (*6*). On this scale, dammar, mastic, and resin AW-2 (Badische Anilin und Soda Fabrik) have a viscosity grade between 1.2 and 1.3 centipoises (cp) whereas Bedacryl 122 X (I.C.I.) and Lucite 44 (du Pont) *n*-butyl polymethacrylate have values about 48. Compared with dammar resin, polymers of high viscosity grade resist flow at a relatively low concentration of solids. As the solvent evaporates beyond this point, the film tends to conform to the contours of the paint surface (*7*). In this manner, a varnish formulated with a resin of high viscosity grade tends to be less glossy than the dammar type, which is able to remain fluid, continuing to level itself, until much more of the solvent has departed.

Among museum authorities, interest in refractive index has centered about the appearance of coatings of polyvinyl acetate. The polymer long used in America, Bakelite vinyl resin AYAF (similar to the earlier Vinylite A), is one of relatively high (80 centipoises) viscosity grade. The formulation of Reid, originally presented by Stout and Gettens, (*8*) was tested in our laboratory and found to give poor distinctness-of-image gloss when it was sprayed on window glass, with the spray gun at a distance of 10 to 20 inches from the glass. In a control test, the gun emitted 35 to 70 ml of toluene per minute. Changes in formulation of the solvent markedly altered the gloss. This laboratory has for several years drawn the attention of museums to polyvinyl acetate polymers of 40- and 9-centipoise viscosity grade (*9*, *10*).

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Effect of Gibberellin on Cell Division in Hyoscyamus

Recently it has been shown that gibberellin, when it is applied to nonvernalized biennial *Hyoscyamus niger* will cause the formation of an elongate stem (*1*). Since the nonvernalized plant grows as a rosette—that is, without measurable internodes—it was suggested that the gibberellin caused an increase in the number of cells. This report presents direct evidence for an increase in cell division resulting from application of gibberellin to biennial *H. niger* (*2*).

Plants of *H. niger* (biennial, purple-flowered strain) were grown from seed in a greenhouse in which the temperature was not permitted to fall below 20°C and in which the photoperiod was maintained at 18 hours by supplementing natural light with artificial illumination. Crystalline gibberellin (*3*) was dissolved in glass-distilled water to which a small amount of a wetting agent (Tween 20) was added. The desired amount of gibberellin was applied at the base of a leaf as close to the apex as possible by means of a hypodermic syringe.

The apical region of the shoot (rosette) was prepared for microscopic examination by fixation in formalin, acetic acid, and 50-percent ethanol (5/5/90); dehydration in tertiary butanol; imbedding in Tissuemat (mp 56°C); longitudinal sectioning at 6 μ; and staining with safranin and fast green according to the procedures outlined by Johansen (*4*). Generally, ten sections per plant, comprising a median slice of 60-μ thickness through the apical region, were examined. Certain restrictions were imposed on this research; only meta-, ana-, and telophase division figures were counted, and only the shoot apex proper and that part of the subapical region which is enclosed by the provascular tissue were examined (see Fig. 1, top). During the period in which observations were made, there was no measurable change in shape and total volume of the subapical region; hence, the cell division counts refer to the same tissue volume.

In one experiment, plants were treated with 0.2 ml of a 25 mg/lit solution of gibberellin (equivalent to a dose of 5 μg per plant) while they were receiving continuous illumination. Illumination was supplied by fluorescent tubes (warm and cool white) yielding approximately 500 ft-ca at plant height, at 23 ± 2°C. In two other experiments, checking the 24-hour point, the plants were treated with gibberellin as described while maintained in greenhouse conditions, (varying temperatures, 18-hour photoperiod). Since the results were substantially the same for all three experiments, the data are grouped together.

As can be seen from Table 1, there was no significant difference between the treated and control plants with respect to the number of division figures in the apical region. However, beginning between 12 and 18 hours after treatment, the number of divisions in the subapical region underwent a striking increase. In this region, a distinction was made between "longitudinal" and "transverse" division figures—that is, division figures the spindle axes of which form an angle of 0 to 45 deg or of 45 to 135 deg with the longitudinal axis of the plant (see Fig. 1, bottom). Table 1 shows that the increase relates mainly to the longitudinal ones; the differences in transverse

division figures between treated and control plants were not significant at the 1-percent level. This effect extended over the uppermost 650 to 800 μ of the subapical region; below this distance, the number of mitotic figures drops rapidly to zero.

The increase of stem growth by gibberellin, the first gibberellin effect observed, and demonstrated in a great number of plants (*5*), is based on an increase in cell length, although in some cases a certain increase in cell number has been considered as probable (*6*). Our results show directly that gibberellin causes a great increase in the number of cell divisions in the subapical region of nonvernalized biennial *H. niger* rosettes, thus proving that gibberellin may function as a regulator not only of cell elongation, but also of cell division.

It is conceivable that the effect of gibberellin on cell division is an indirect one, the division being induced by accelerated cell elongation. Dividing cells in the subapical region of *H. niger* are indeed 1.5 times as long as nondividing ones. However, this is equally true of treated and untreated plants, and the length of cells is not increased even after 9 days of daily gibberellin applications, although their shape is then quite different. It thus seems that increased cell elongation follows rather than precedes the effect of gibberellin on cell division.

The data presented in Table 1 further indicate a directional influence of gibberellin on cell division, longitudinal division figures being increased to a much greater extent than transverse ones. The factors responsible for this effect require further investigation.

It will also be necessary to check in further experiments whether, as suggested by the ones reported here, gibberellin fails to increase cell division in the apical region of the *H. niger* shoot. If this situation is generally true, it is suggestive of the hypothesis of Buvat (*7*), according to which the extreme apical region of the shoot meristem does not participate in vegetative growth, the actual meristematic activity being localized below that region. This area of meristematic activity, called the *méristème medullaire*, corresponds to the lower part of the apical and the upper part of the subapical region of *H. niger*. However, Buvat's theory goes further and describes the *méristème medullaire* and not the extreme apex as the origin of the initial cells of the entire stem (*7*, see particularly Fig. 12), whereas our results by no means exclude the apex as the primary source.

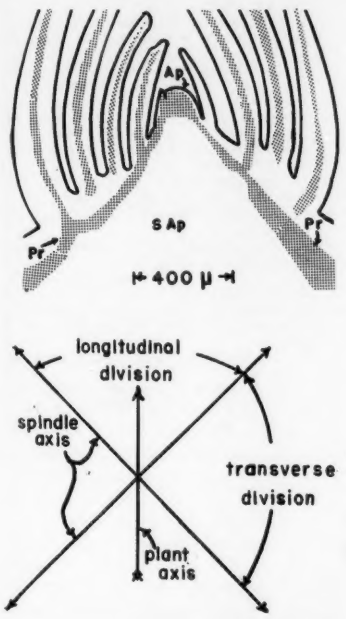

Fig. 1. (Top) Semidiagrammatic drawing of the shoot of nonvernalized, biennial *Hyoscyamus* plant. Ap, apical region; SAp, subapical region; Pr, provascular tissue. (Bottom) Sketch showing the basis for selection of longitudinal and transverse cell division figures.

Table 1. Effect of gibberellin on cell division in biennial *H. niger*. All figures represent the number of division figures per 60-μ tissue slice. The errors quoted are the standard errors of the mean.

Hours after application of gibberellin	Apical region	Subapical region		Number of plants
		Longitudinal division figures	Transverse division figures	
		Controls		
0	12 ± 2	2 ± 1	3 ± 1	5
6	12 ± 1	3 ± 1	4 ± 1	4
12	15 ± 2	1 ± 0.5	4 ± 0.5	5
18	15 ± 3	1 ± 1	3 ± 1	5
24	9 ± 3	3 ± 0.5*	8 ± 2	10
		5 μg *of gibberellin*		
6	8 ± 1	3 ± 1	6 ± 1	5
12	13 ± 2	3 ± 2	6 ± 2	5
18	11 ± 1	12 ± 4	11 ± 2	5
24	12 ± 1	29 ± 3*	10 ± 2	9

* The difference is significant at the 1-percent level using the *t* test for unpaired samples in which the variances for the parent populations are unequal; described by Stearman (*8*, pp. 182 and 183).

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12 March 1957

Proposed Mechanism of Action of Hydrolytic Enzymes

Certain hydrolytic enzymes, notably chymotrypsin, trypsin, and acetylcholinesterase have been shown to react with reagents such as diisopropylfluorophosphate to yield inactive proteins which contain single diisopropylphosphate residues (*1*, *2*). The inactive protein is relatively stable in water but may be converted into the active enzyme by treatment with a variety of nucleophilic reagents (*3*). Chemical or enzymatic hydrolysis of the inhibited protein has invariably shown the dialkylphosphate residue to be attached at the hydroxyl group of a single serine residue (*4*).

Recently, singly substituted, inactive, acyl derivatives have been successfully prepared by reaction of delta-chymotrypsin with compounds such as *p*-nitrophenyl acetate, acetic anhydride, and benzoyl chloride (*5*). These proteins appear to be very similar to the dialkylphosphate-substituted enzymes except that they are more readily reactivated by water. These facts, together with the close parallel of the *p*H dependence of acylation (*5*, *6*), normal hydrolytic activity (*7*), and dialkylphosphorylation (*1*), have led to the conclusion that these reactions are closely related and involve directly at least a portion of the active center of the enzymes (*3*). Dixon and Neurath (*5*) have also shown that the pK' for acylation and deacylation of delta-chymotrypsin are different, being about 6.2 and 6.8, respectively. The latter value is very close to that reported

for the hydrolysis of acetyl-L-tryptophan and acetyl-L-tyrosine ethyl ester, 6.71, by the enzyme (7). All these values fall in a *p*H region associated with the ionization of imidazole nitrogen. This fact, together with the almost inescapable conclusion that the mechanism involves nucleophilic attack on the carbonyl function of the natural substrates (*2, 3, 8*) has led to the idea that the uncharged imidazole nitrogen is the primary nucleophilic agent.

The location of the dialkylphosphate residue on the serine hydroxyl has been explained as the result of a secondary transfer reaction (*9*). The fact that the heat of ionization of the group of *pK'* 6.71 referred to in the preceding paragraph is about 11 kcal mole^{-1} (*7*) rather than the 6 to 7 kcal mole^{-1} ordinarily encountered for imidazole would, however, suggest that a relatively uncomplicated nucleophilic attack by the imidazole nitrogen is not a satisfactory explanation. It would seem that a mechanism should be sought which includes the direct involvement of the serine hydroxyl.

Such a mechanism is suggested in the condensed scheme outlined in Fig. 1. The formation of the active center is postulated to involve hydrogen bond formation between the serine hydroxyl and an uncharged imidazole nucleus (*10, 11*). The two components could be located on separate peptide chains in the enzyme as long as the specific three-dimensional structure, formed during activation of the zymogen, brought them near enough for this interaction to occur. The polarization of the resulting structure would cause the serine oxygen to be the nucleophilic agent which attacks the carbonyl function of the substrate (*3, 8, 11*).

The complex is stabilized by the simultaneous "exchange" of the hydrogen bond from the serine oxygen to the carbonyl oxygen of the substrate. Another group capable of hydrogen bonding could be involved in this sequence, for we have so far been unable to determine satisfactorily whether or not steric considerations preclude the involvement of a single imidazole nucleus as shown.

The *p*H dependence of this step would be that associated with the acylation reaction. Thus, the *pK'* would be 6.2 and the heat of ionization might be expected to be low, near 1 or 2 kcal mole^{-1}. The intermediate acylated enzyme is written with the proton on the imidazole nitrogen. The deacylation reaction involves the loss of this positive charge simultaneously with the attack of the nucleophilic reagent, abbreviated Nu:H. This reaction would therefore be expected to show a *p*H dependence related to imidazole ionization, but the heat of ionization might be expected to be considerably different.

This, as has been noted, is the actual situation. The relative magnitude of the two *pK'* values is in accord with the demonstrated stabilization of the acylated enzyme at low *p*H (*12*). A possible alternative route of deacylation (*13*) would involve the nucleophilic attack of the imidazole nitrogen on the newly formed ester linkage of the postulated acyl intermediate, leading to formation of the acyl imidazole. The latter is unstable in water, hydrolyzing rapidly to give the product and regenerated active enzyme.

The reaction of alkylphosphates in such a scheme may be written in an entirely analogous manner, except that the resulting phosphorylated enzyme would be less susceptible to deacylation through nucleophilic attack (*3, 14*).

The validity of any mechanism rests on its agreement with available data, its success in predicting the results of subsequent new tests, and chemical and physical studies directed toward establishing the presence of specific molecular groupings invoked in the reaction scheme. The agreement of the proposed mechanism with existing data has been discussed. It is hoped that consideration of this alternative to what might be termed the "primary imidazole" hypothesis may lead to direct tests for distinguishing the two, though an approach does not seem to be immediately obvious. Although determination of the heat of ionization for the *p*H-dependent step preceding acylation may be of value, it does not seem likely that the formation of the hydrogen bond in the active enzyme would be detectable.

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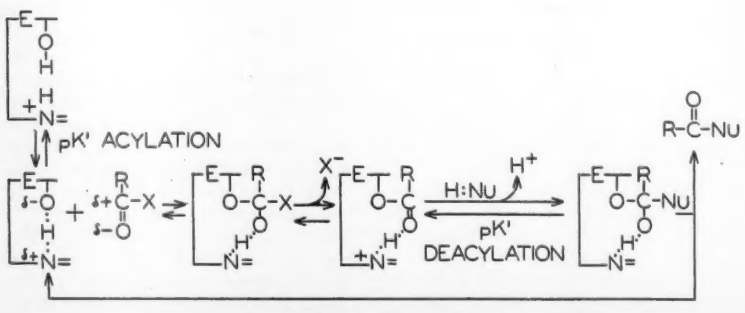

Fig. 1. Proposed mechanism for enzymatic hydrolysis.

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21 March 1957

Time Course of Far-Red Inactivation of Photomorphogenesis

Flint and McAlister (*1*) demonstrated in 1935 that red and far-red radiant energy produced opposing effects on lettuce-seed germination; the red stimulated germination and the far-red inhibited it. Borthwick *et al.* (*2*) later showed that, if the far-red were applied subsequent to the red, it prevented the consequences of the red reaction. They called this phenomenon photoreversal. The red induction and potentiality for its far-red photoinactivation also has been demonstrated in photomorphogenic development of seedlings (*3, 4*) and photoperiodism (*5*). Hendricks *et al.* (*6*) have advanced the hypothesis that the system involves a photoreversible pigment with two stable electronic energy states. When it is in the one energy state, the pigment can be transferred to the other if a quantum in the absorption band characteristic of the first state is absorbed. It can then be reversed to the original state, presumably by way of the same pathway, by the absorption of a quantum characteristic of the second state. Hendricks *et al.* postulate that the reaction rate is not dependent on a mo-

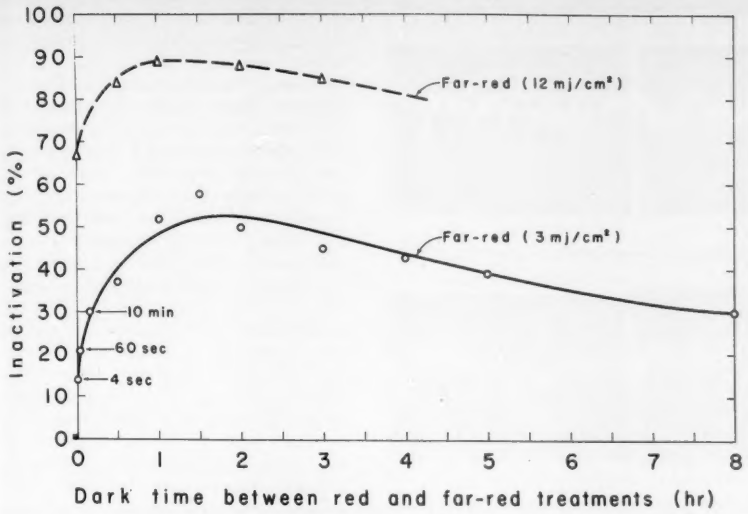

Fig. 1. Time course of far-red inactivation of red-induced morphogenesis in the hypocotyl hook of the bean seedling. Curves are shown for energy levels of 3 and 12 mj/cm², applied at 1000 μw/cm² for 3 and 12 seconds, respectively.

lecular collision in either direction and that both photoreactions follow first-order kinetics.

If such a simple reversal obtains, with no intervening collision step, it seems logical to assume that the system would be immediately reversible at the maximum rate, and that the time course would show a constant value of reversibility, to the point where the consequences of the red induction result in irreversible growth reactions.

In view of these considerations, it was decided to determine the time course for photoinactivation of red-induced photomorphogenesis in the bean seedling (*7*). A high-intensity carbon arc, in combination with interference filters, was used as the source. The irradiation periods were as short as could be obtained with this system, and were a matter of seconds. The bioassay was the rate of opening of the hypocotyl hook of bean, the technique of which has been described by Klein *et al.* (*8*). In this system, the induction response has a peak of activity in the red at 660 mμ, and photoinactivation peaks at 710 and 730 mμ (*3*). The angle of hook opening is proportional to the logarithm of the incident red energy over an irradiance range of at least 1 million for short periods of photoinduction, and the inactivating effect of the far-red is directly proportional to irradiance. A total energy of 10 mj/cm² of far-red energy distributed over a 30-minute period produces about maximal photoinactivation, the percentage of inactivation rising linearly with energy to approximately 85 percent and then leveling off rapidly thereafter.

The hypocotyl hooks were excised from 6-day old Black Valentine bean seedlings and arranged in a circle on moist filter paper in a 150-mm petri dish. The excised hooks were exposed to red energy at 25° with a carbon arc for 3 minutes at an irradiance of approximately 1500 μw/cm², which yielded a total energy of 250 mj/cm² at 660 mμ. The hooks were then kept in the dark until time for the far-red exposure, which was given at approximately 1000 μw/cm² at 730 mμ for 3 and 12 seconds for total energies of 3 and 12 mj/cm², respectively. The two filter systems were mounted in a sliding panel so arranged that the shortest dark time was 4 seconds.

The results are given in Fig. 1 as time-course curves. It will be noted that the capacity for photoinactivation by the far-red increases rapidly with time, reaching a maximum at between 1 and 2 hours and then decreasing gradually. The decrease is consistent with the hypothesis that irreversible growth reactions have occurred. For the shortest periods of time, the percentage inactivation is approximately proportional to the far-red energy. Data are available (*9*) which show that the far-red is incapable of producing significant inactivation at proportionately low energy levels in the presence of the red. Therefore, it is probable that the curve falls back to zero, either at zero time or slightly prior to the end of the red-induction period.

These results suggest that a thermochemical step intervenes between the absorption of red photons and maximum capacity for inactivation by the far-red. There are several possibilities about the nature of this step. It may involve the direct modification of the pigment itself to a far-red absorbing form so that inactivation cannot proceed until thermal conversion occurs. On the other hand, it may be concerned with synthesis of a reactant essential to the completion of the inactivation step, the concentration of which limits the far-red reversal process. The complete system is being studied with a complex of variables of incident energy, time, and temperature, with the view of determining the nature of the intervening step.

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13 March 1957

Some Characteristics of Cortical Recruiting Responses in Unanesthetized Cats

In 1941, Morison and Dempsey (*1*) demonstrated that trains of 8- to 12-per-second stimuli delivered to the intralaminar thalamic nuclei of the anesthetized cat evoked long-latency, surface-negative potentials which were widely distributed over the cerebral cortex. Because the first stimulus of the train evoked little or no cortical response, and because the responses to each successive stimulus showed a progressive increase in amplitude to a maximum, these potentials were termed "recruiting responses." Subsequent investigations have further defined the thalamocortical pathways and the character of the synaptic connections which mediate recruiting responses (*2–4*). It was shown that pentobarbital lowered the threshold for recruiting responses (*5*), and, since stimulation of the brain-stem reticular formation prevented their occurrence (*6*), it was assumed that recruiting responses could not be obtained in the waking animal.

The study described in this report employed the technique of chronic implantation of electrodes, which was developed by Sheatz (*7*), to explore this

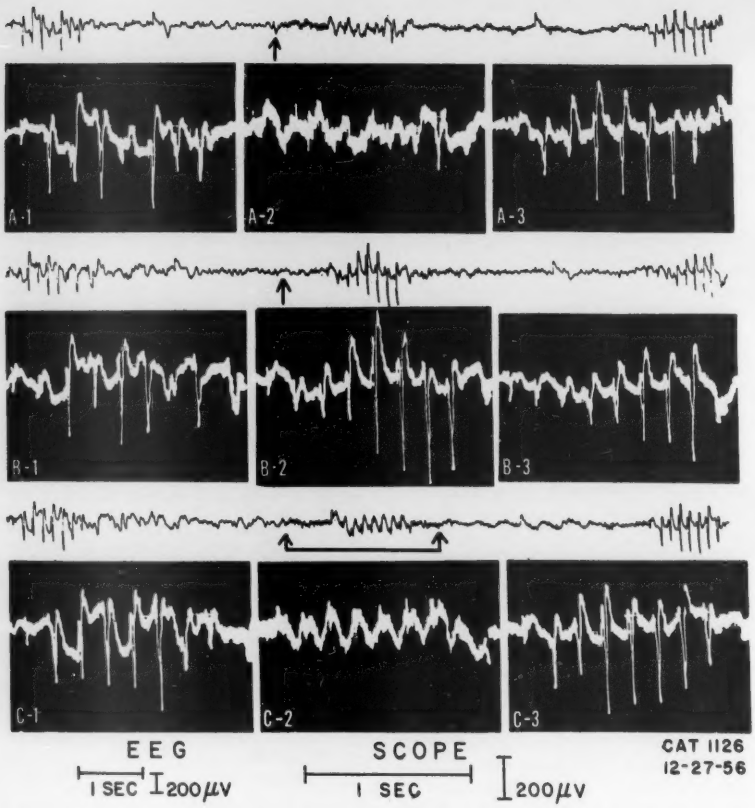

Fig. 1. Recruiting responses in unanesthetized cats. Electroencephalographic records (above) and corresponding oscillographic traces (below) show the recruiting responses recorded from the anterior suprasylvian gyrus following 6-per-second submaximal stimulation of the ipsilateral center median nucleus. *A*-1 and *A*-2, responses recorded before (*A*-1) and after (*A*-2) a noise, which occurred at the arrow. The rapid return of recruiting responses to normal amplitude following the noise is shown in *A*-3. *B*-2, failure of the noise (at arrow) to reduce recruiting responses following repeated presentation of this stimulus. (Bottom row) Recruiting responses before (*C*-1), during (*C*-2), and after (*C*-3) 100-per-second stimulation of the brain stem for 2.5 seconds. The period of brain-stem stimulation is indicated by the solid line between the two arrows (positive is up).

matter further. It was found that stimulation of the intralaminar nuclei may evoke well-developed recruiting responses in the normally waking animal. Figure 1 shows such responses evoked in the anterior suprasylvian gyrus by submaximal 6-per-second stimulation of the ipsilateral center median nucleus. At the time when these responses were recorded, the cat was sitting up in its cage with an alert appearance, occasionally looking about. No detectable behavioral alterations were associated with the recruiting responses. With more intense stimuli, a variety of behavioral alterations resulted, some of which were similar to those described by Hunter and Jasper (*8*). When a loud noise was made, there was a marked decrease in the amplitude of the recruiting responses (Fig. 1, *A*-2). Within 5 seconds of this auditory stimulus, however, responses had returned to original amplitude (Fig. 1, *A*-3). Repeated exposure of the animal to the originally effective auditory stimulus was associated with a gradual disappearance of its blocking effect, as had been previously shown by Jasper *et al.* (*3*). Figure 1, *B*-2, shows this failure of the same auditory stimulus to cause reduction of recruiting responses following habituation. Figure 1, *C*-2, demonstrates the reduction in the amplitude of recruiting responses which results from stimulation of the brain-stem reticular formation. Unlike the effects of the auditory stimulus, the effects of the brain-stem stimulus did not become attenuated with repeated presentation of the stimulus. The effects of brain-stem stimulation were, however, abolished by anesthetic doses of pentobarbital.

Contrary to the expectations based on previous work, therefore, it has been found that the presence of a "desynchronized" electroencephalogram and of behavior indicative of an alert waking state is not incompatible with the induction of recruiting responses. Under such circumstances, these responses can be reduced or prevented by novel, peripheral afferent stimuli or by stimulation of the brain-stem reticular formation. The behavioral changes which were associated with reduction of recruiting responses appeared to range from a shift or attraction of attention (either "spontaneous" or as a result of an afferent stimulus), through brief startle, to more enduring and pronounced excitement. The prevention of evoked recruiting responses in the waking animal may thus be analogous to the blocking of the alpha rhythm in the human electroencephalogram. In man, alpha activity is not prevented by the waking state and may similarly be blocked by a shift or focus of attention as well as by more marked arousal.

More generally, these observations emphasize the undesirability of drawing inferences concerning behavior from electrophysiological observations in the anesthetized or immobilized animal which is incapable of any behavioral display. This is true not only in the case of the recruiting responses but is equally relevant for the response to stimulation of the brain-stem reticular formation. The effects of brain-stem stimulation have customarily been given blanket equation with awakening (*4*), but depending on the state of the animal and the parameters and location of stimulation, such stimulation would appear to be capable of leading to a wide spectrum of behavioral changes that range from awakening to the evocation of attention, to startle, or to the arousal of generalized excitement. Now that appropriate techniques are available, it is to be hoped that such inferences may give way completely to observations of behavior.

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Lithium, Sodium, and Potassium in D-α-Hydroxy Fatty Acid Metabolism of Lactobacillus casei

D-α-Hydroxy fatty acids are presumably of considerable neurophysiological importance because of their prominent occurrence in essential structural lipids (cerebrosides) of mammalian brain and nervous tissues (*1*). It is of interest, therefore, that these acids are also known to occur in microbial cerebrosides (*2*) and to promote growth of *Lactobacillus casei* 280-16 (*3*). The latter, a mutant strain apparently normal in all respects except for its inability to racemize the L-lactic acid it produces by fermentation (*3*), has recently been observed to undergo spontaneous dissociation (*4*), yielding two distinct substrains. The first of these, strain 260-16A, appears to be identical with the original strain 280-16 (before dissociation), whereas the second strain, 280-16B, is capable of good growth in hydroxy acid-free media but may be selectively inhibited by l-tetradecene under these conditions (*4*).

The following has seemed likely from available evidence (*3, 4*). (i) A long-chain D-α-hydroxy fatty acid (such as those known to occur in microbial cerebrosides) constitutes an indispensable component of an essential lipid (perhaps a cerebroside) in *L. casei*. (ii) This fatty acid is normally produced through a metabolic pathway commencing with either D-lactic acid (which is produced by the parent strain but which must be provided for strain 280-16A) or some other relatively short-chain D-α-hydroxy fatty acid (those of from 4 to 14 carbon atoms may be utilized in place of D-lactic acid by strain 280-16A). (iii) An alternative pathway, in which the relatively short-chain D-α-hydroxy fatty acids do not function as intermediates but through which the essential long-chain D-α-hydroxy fatty acid may be synthesized, is available in strain 280-16B. (iv) The alternative pathway, but not the normal pathway, includes at least one step which is inhibited by l-tetradecene.

It now appears, from the results of experiments described in this report (*5*), that (i) the alternative pathway includes at least one step which is markedly inhibited by potassium ion; (ii) this pathway is potentially available in strain 280-16A and probably also in the parent strain as well as in strain 280-16B; and (iii) the latter strain has acquired, through mutation, an increased tolerance to potassium, thus accounting for its ability to grow in certain hydroxy acid-free media that fail to support growth of strain 280-16A.

The results shown in Table 1 were obtained under the experimental conditions described previously (*4, 6*) except that the potassium phosphates in the basal medium were replaced with equimolar amounts of the corresponding sodium phosphates. It may be seen (Table 1) that, whereas strain 280-16A failed to grow appreciably in unsupplemented hydroxy acid-free medium with potassium levels greater than 8 μmole/ml, (*7*), it produced considerable growth at potassium levels of either 1 or 2 μmole/ml, and it is evident that the results with strain 280-16A were essentially the same as those with strain 280-16B except that greater concentrations of potassium ion were required to inhibit growth of the latter organism. The inhibitory effects of potassium ion were markedly antagonized by either lithium ion at relatively low concentrations or sodium ion at considerably higher concentrations (Table 1). These results suggest that lithium ion may have a catalytic function in one or more steps of the alternative metabolic pathway and that it is this function which is inhibited by potassium ion. Sodium ion apparently either replaces lithium ion or indirectly antagonizes the effects of potassium.

When the basal medium employed previously (*4, 6*) (sodium and potassium at basal levels of 71.5 and 9.4 μmole/ml, respectively) was supplemented with 0.12 μmole of either DL-lactic acid or DL-α-hydroxylauric acid per milliliter (hydroxy acids of intermediate chain lengths were not tested but would be expected to be similarly effective), strains 280-16A and 280-16B were not inhibited by potassium chloride at 200 μmole/ml after 52 hours' incubation, whereas complete inhibition of these strains was effected under the same conditions when the hydroxy acid supplement was omitted. The parent strain of *L. casei* was not inhibited by potassium even in unsupplemented media, as was to be expected since this strain is able to produce D-lactic acid in excess of its nutritional requirements.

The conclusions set forth in this report are to be regarded as tentative until the experimental work now in progress is completed. The apparent involvement of lithium, sodium, and potassium ions in the biosynthesis of bacterial D-α-hydroxy fatty acids suggests, nevertheless, that these ions may similarly influence the biosynthesis of mammalian cerebroside acids and that normal maintenance of important lipoidal structural materials such as myelin (*8*) might, therefore, be dependent on an appropriate balance of the ions.

Table 1. Response of *L. casei* 280-16 substrains to lithium, sodium, and potassium chlorides in D-α-hydroxy acid-free medium.

Potassium chloride supplement (μmole/ml)	No supplement	Sodium chloride supplement (μmole/ml)*			Lithium chloride supplement (μmole/ml)†		
		100	300	500	12	24	48
		Response of substrain A‡					
0	1.6	2.0	1.2	1.0	1.5	1.4	1.4
1	11.0	12.0	9.4	2.1	12.2	12.0	11.2
2	11.9	13.9	13.0	9.4	13.9	14.0	13.6
4	9.3	12.2	15.0	13.5	11.8	12.6	13.0
8	3.0	9.5	13.4	12.7	10.3	11.4	12.6
32	1.1	5.0	9.1	10.2	6.0	10.6	12.5
128	1.0	2.5	5.1	6.6	2.0	6.7	10.4
		Response of substrain B‡					
0	1.6	1.5	1.3	1.1	1.7	1.6	1.8
1	14.1	13.0	11.4	6.3	13.1	13.2	11.5
2	16.1	15.9	15.3	12.0	16.1	16.0	16.2
4	15.1	14.9	15.5	13.8	15.3	14.3	15.7
8	13.7	13.7	14.1	13.6	14.7	15.1	15.3
32	9.9	9.0	10.6	11.9	12.0	12.8	14.8
128	2.1	3.3	8.6	9.8	3.1	8.0	11.3

* These amounts are in addition to the basal sodium content of 81 μmole/ml.
† Marked inhibition was effected at concentrations of 96 μmole/ml and more.
‡ Measured after 38.5 hours' incubation at 35°C. The values representing growth response are in terms of milliliters of 0.01*N* sodium hydroxide required to titrate 1 ml of test culture.

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References and Notes

1. The distribution of cerebrosides has been discussed by H. J. Deuel, Jr. [*The Lipids* (Interscience, New York, 1955), vol. 1, pp. 473–475]. That the cerebroside hydroxy acids are of the D-configuration has been established by D. H. S. Horn and Y. Y. Pretorius [*J. Chem. Soc.* 1954, 1460 (1954)], and by K. Mislow and S. Bleicher [*J. Am. Chem Soc.* 76, 2825 (1954)].
2. Yeast cerebrin, the principal cerebroside of yeast, has been extensively studied by F. Reindel and his coworkers [*Ann. Chem. Justus Liebigs* 480, 76 (1930); 544, 116 (1940)]. That the yeast cerebronic acid has the same optical configuration as that of brain cerebronic acid is evident from the data of A. C. Chibnall *et al.* [*Biochem. J.* (*London*) 55, 707, 711 (1953)].
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of California. We acknowledge the valuable technical assistance of Evelyn Brown, Janet Frazer, and Tibor Batonay.

6. Tween 40 (Atlas Powder Co.) was included in the test media at 4 mg percent.
7. Media used previously in this laboratory have contained potassium at concentrations not less than 9.4 μmole/ml.
8. It is evident from the data of J. Folch-Pi [in *Biochemistry of the Developing Nervous System*, H. Waelch, Ed. (Academic Press, New York, 1955), pp. 124–125] that the appearance of cerebrosides parallels myelination in developing mouse brain and from the report of J. N. Cumings [*Brain* 76, 551 (1953); 78, 554 (1955)] that demyelination in multiple sclerosis is accompanied by a proportionate loss of cerebrosides.

8 March 1957

Autoradiography of Volcanic Rocks of Mount Lassen

Following the procedure of Guilbert and Adams (*1*), an autoradiographic study has been made of the volcanic rocks of Lassen Volcanic National Park, California. By this method, the sites of alpha-emitting elements (thorium and uranium series) may be located within 5 μ in thin sections. In each of the sections studied, approximately 100 alpha tracks were counted, and the mineral from which each one emanated was identified. These data, plus a modal analysis of the section, permitted calculation for each mineral of the following ratio: percentage of alpha tracks from mineral/percentage of mineral in the rock (*2*). Table 1 shows these ratios, plus the modal percentages, for the minerals in each section studied (*3*).

In Table 1, for each mineral in each sample, the upper (italic) figure in each pair is the ratio of percentage alpha tracks from mineral/percentage of mineral in the rock; and the lower figure (roman) is the modal percentage of the mineral. All samples had previously been used by Adams (*4*) in a study of the uranium geochemistry of the Mount Lassen lavas.

The volcanic rocks studied consisted of phenocrysts of plagioclase and one or more ferromagnesian minerals (and rarely quartz) in a groundmass of glass or aphanitic material. As shown by Table 1, the determined ratios (percentage alpha tracks from mineral/percentage of mineral in the rock) are close to 1 for most minerals, including glass, in each sample. Apparently no mineral is either enriched or impoverished in thorium and uranium, and the distribution of alpha-emitting elements seems to be uniform.

In addition to the minerals listed in Table 1, most samples contained small amounts of magnetite, and some samples contained a few tiny grains of apatite; no alpha tracks were definitely associated with the apatite, and we were not able to detect tracks in the emulsion above the opaque magnetite. The maximum number of alpha tracks from uncertain sources (for example, within 5 μ of the edges of grains) was 11 percent for all sections shown in Table 1. The possibility that thorium and uranium are concentrated in minerals so scarce that they do not appear in the sections studied is apparently eliminated by the fact that the total number of alpha tracks in the emulsion over each section accounts for roughly half of the radiometrically determined alpha activity for each sample.

In two samples not shown in Table 1, the constituents of the groundmass were sufficiently coarse so that alpha tracks could be identified from individual phases (glass, pyroxene, and plagioclase). Minerals in the groundmass apparently contained the same concentration of thorium and uranium as the corresponding phenocrysts, though the small grain size increased the uncertainty of location of the alpha tracks.

It must be concluded that the alpha-emitting elements are uniformly distributed among all the various constituents in the volcanic rocks of Mount Lassen. Apparently the rapid solidification of the lavas under volcanic conditions caused entrapment of the thorium and uranium in all the mineral phases and prevented concentration of these elements in any single mineral (*5*).

Table 1. Autoradiographic data and modal analyses of the volcanic rocks of Mount Lassen.

Sample No. (*3*)	Minerals						
	Phenocrysts						Groundmass
	Plagioclase	Hornblende	Pyroxene	Biotite	Quartz	Altered ferromagnesian	
5	*0.74*	*2.4*		*11.0*			*0.96**
5	19.5	4.3		0.2			76.0 *
8	*1.1*	*0.97*	*1.6*	*0.65*			*0.97**
8	25.3	0.9	3.4	2.6			67.0 *
11	*1.1*	*1.6*	*1.6*	*4.2*			*0.93*†
11	25.9	2.2	0.7	0.3			69.9 †
14	*0.48*	*2.5*	*1.5*	*6.9*			*1.2* †
14	27.9	1.3	2.8	0.1			67.6 †
15B	*1.0*		*1.2*				*0.94**
15B	60.4		11.0				28.6 *
16	*1.0*	*2.3*	*4.1*	*1.1*	*0.75*	*0.0*	*0.97*†
16	30.0	2.2	0.5	1.9	2.7	2.3	59.5 †
17	*0.95*	*3.0*	*1.0*				*1.2* †
17	77.5	0.7	10.9				10.2 †
18	*0.70*		*1.7*				*0.99*‡
18	5.6		3.4				90.9 ‡
21	*1.7*		*0.62*		*0.57*		*0.80*†
21	28.8		11.9		13.3		45.9 †
24	*0.95*	*1.1*	*1.0*				*1.0* †
24	17.3	1.0	7.0				74.8 †
25	*3.5*		*1.3*				*0.92*†
25	0.6		17.5				82.0 †
31	*1.0*		*0.85*				*2.4* *
31	65.9		29.2				4.9 *
36	*0.99*	*1.1*	*0.99*				*1.4* ‡
36	64.0	0.9	28.3				6.4 ‡
39	*0.86*		*0.0*			*1.4*	*1.05*†
39	19.0		1.8			1.0	77.9 †
41A	*0.92*	*1.5*	*0.98*	*2.8*			*0.99*†
41A	41.3	0.7	13.1	1.0			42.7 †

* Glass. † Glass (with plagioclase). ‡ Plagioclase, pyroxene, and glass.

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1. J. M. Guilbert and J. A. S. Adams, *Nucleonics* 13, No. 7, 43 (1955).
2. For both alpha counts and modal analyses, traverses were spaced so that the entire section was covered.
3. Sample numbers represent the following rocks: 5—Manzanita dacite; 8 and 11—Raker Peak dacite; 14—Chaos Crags dacite; 15B—Table Mountain basalt; 16—Chaos Jumbles dacite; 17—Flatiron andesite; 18—Pilot Mountain andesite; 21—quartz basalt bomb; 24—vesicular basalt, Cinder Cone; 25—andesite, Painted Dunes; 31—Eastern basalt; 36—Raker Peak pyroxene andesite; 39—altered Flatiron andesite; 14A—andesite.
4. J. A. S. Adams, *Geochim. et Cosmochim. Acta* 8, 74 (1955).
5. This work was supported by the Robert A. Welch Foundation, grant C-009. We express our thanks to F. W. Fessenden, J. A. Ragsdale, and J. P. Shannon for their help.

18 March 1957

Book Reviews

The Species Concept in Palaeontology. Systematics Association publication No. 2: A symposium. P. C. Sylvester-Bradley, Ed. Systematics Association, London, 1956. 145 pp. Illus. $2.

In 1940 the Systematics Association published its first symposium, *The New Systematics*. It is true, as some critics have commented, that the origins of the new systematics can be traced back another century or so, and no doubt some enterprising classicist will produce an ancient Greek forerunner. Nevertheless, that publication did signalize and stimulate a true revolution in the science of systematics—a change, to state it in the briefest possible terms, from the classification of idealized, fixed types (typology) to the classification of real, varying populations. Since 1940 the new point of view, with its new methods and results, has become usual among students of living organisms.

Now, the second symposium of the Systematics Association demonstrates, among other things, how far the new systematics has affected the study of extinct organisms and to what extent different problems appear in this field. Eighteen paleontologists and zoologists, all but one of whom (Newell) is British, have contributed to the discussion. Almost all of them make the point, implicitly at least, that paleontological systematics is inherently more complex and difficult than neontological systematics. There is, in the first place, the added dimension of time. There is, moreover, a whole series of special difficulties related to paleontological sampling, which are here well discussed by Rhodes, Newell, and George, among others.

Apart from such useful treatments of methodological problems and a few oddities, such as Haldane's washing his hands of the stated topic, the main issues seem to be two: the applicability of population concepts to fossils and the problems that are connected with classifying lineages through time. The interplay of questions that bear on the first and broader of these issues is somewhat obscured by organization and terminology. The body of the book is divided into sections labeled "Theory" and "Practice," a distinction that is seldom valid in science and is rejected by some of the authors here involved. In fact, the distinction achieved is not between theory and practice but between two purposes and attitudes. The nominal "theoreticians" are interested in fossils as organisms, including their "practical" applications. The nominally "practical" students are interested in stratigraphy more than in organisms as such. It is not surprising, then, that the writers on "theory," notably Thomas, Rhodes, Westoll, Newell, and Joysey, are unanimous in welcoming population concepts in systematics, while the writers on "practice," notably Arkell and Eager, mainly support a type systematics. Indeed, this is no question of theory and practice but the same issue that has been fought out since 1940 (and before) in neontology between population systematics and typology.

This issue is somewhat compromised, not only by the false tendency to equate typology with "practical" paleontology, but also by the foreword of the chairman (White). He remarks: "It is true that there is a satisfactory degree of unanimity among those . . . often unembarrassed by prolonged or wide practical experience . . ." and "Fresh breezes are doubtless blowing through the musty halls of orthodox paleontology, but some of us may be forgiven for thinking that in places the amount of wind is excessive"—statements that contributors to the symposium may find discourteous and readers will surely find unjustified. There is a further ambiguity in the usages throughout the book of the term *morphospecies*, which sometimes means a real, biologically significant population that is recognized on morphological evidence and, sometimes, an idealistic grouping on the basis of resemblance to an arbitrary type, with consequent haziness of logical grasp of the differences between these two concepts. In spite of editorial bias and of some logical confusion among their opponents, it is clear from the book as a whole that, in paleontology as in neontology, the typologists are now the old guard still fighting a lost battle. It is even clear, although here not perhaps as fully demonstrated as it could be, that the supreme argument of the typological stratigraphers is flatly fallacious. Population systematics is demonstrably superior for the most fully practical stratigraphic applications.

The problem of ancestral-descendent species (if such they should be called) successive through time is peculiar to paleontology and is here considered at some length, especially by Thomas, Rhodes, Westoll, Newell, Joysey, Kermack, and George. There is not complete agreement, but there is a consensus that there are available sensible criteria for specific subdivision of these continua and that the units so achieved may be arbitrary but are not, as has been claimed, "unreal."

Authors not previously named are Parker, Ager, Parkinson, Melville, Smout, McKerrow, and Sylvester-Bradley, who has supplied a stimulating introduction. There are a meager index and a good glossary. The latter, as glossaries so often do, raises the question whether some terms are really necessary.

It is not likely that the Systematics Association's second symposium will achieve the fame and influence of the first. This book is, nevertheless, another important milestone, indispensable for all paleontologists, zoologists, and evolutionists.

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Metallurgy of Chromium and Its Alloys. vol. II of *Chromium*. Marvin J. Udy, Ed. Reinhold, New York; Chapman & Hall, London, 1956. 402 pp. Illus. $11.

The metallurgy section of the monograph on *Chromium* represents the efforts of a number of eminent contributors, each of whom is a recognized expert in his particular field. The result is a comprehensive coverage of the various phases of the extractive metallurgy of chromium and of the properties of chromium, its alloys, metallurgical uses, and its uses in refractories.

The section on the extractive processes for chromium covers these methods very well and goes into great detail about the prevailing commercial processes, thus providing the reader with full information about the subject. For one concerned with the pure metal, however, the information which is included is somewhat meager.

The physical properties of the metal are given in excellent detail; thus, the book is excellent for purposes of reference. Also, the behavior of chromium in various steels, cast irons, high temperature alloys, electrical resistance alloys, and nonferrous alloys is described in detail by competent specialists in these several fields of endeavor. However, current investigations concerning chromium-base

alloys—a subject of considerable current interest—receive but scant attention.

The characteristics of chromite which are responsible for its refractory properties, as well as the processing of the ore to refractory products and the specific applications, are discussed in excellent detail in the final section of the monograph. The volume is thus a handy reference book for those interested in furnace linings and similar applications.

From an editorial standpoint, it is apparent that the individual chapters are by different authors. Some are excellently well edited, while others need more careful editing and proofreading.

In general, this is an excellent treatise, though it is somewhat weak, for a 1956 publication, in its coverage of the most recent developments.

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Energy and Structure in Psychoanalysis. Kenneth Mark Colby. Ronald Press, New York, 1955. ix + 154 pp. Illus. $4.50.

Books on psychoanalysis usually deal with its clinical theory; the most comprehensive one, Fenichel's, indicates this limitation by its title, *The Psychoanalytic Theory of Neurosis*. There exists, however, a fragmentary—yet consistent—general theory of psychoanalysis, which comprises the premises of the special (clinical) theory, the concepts built on it, and the generalizations derived from it. Since this general theory deals with what in Freud's time was *beyond* the scope of academic psychology, and since in relation to the clinical one it is a metatheory, it was named *metapsychology*. It is hardly ever mentioned in books written for nonspecialists; even books written for the specialist seldom do more than touch on it.

In the battle fought over the special theory, the foundations Freud laid for the general theory were scarcely noticed by the antagonists, and its adherents seem to have been too busy to systematize, develop, or use it. Only since the late 1930's has interest in it slowly revived. It is quite possible that the gap between experimental psychology and psychoanalysis, which has remained unbridged in spite of ever-increasing rapprochement, mutual interest, and much earnest work on both sides, is due in part to the undeveloped state of the general theory. It has happened before that the integration of two branches of a science was delayed until the theory of one or both reached a sufficient level of generality. Be this as it may, the special (clinical) theory of psychoanalysis remained all but intractable to the methods of experimental psychology, although the weight of amassed observations is such that the validity of the core of this theory can no longer be questioned.

Kenneth Colby's small volume focuses on the general theory. It is directed "not only to psychoanalysts, but to all theoreticians of those fluid borderlands between the psychological, biological, and sociological sciences" (p. v) and calls general attention to those rarely studied writings of Freud, which are the major sources of this general theory: the "Project for a scientific psychology," the seventh chapter of *The Interpretation of Dreams*, "On narcissism: an introduction," and "The unconscious." The book has two further merits. First, it tackles some of the thorniest problems of metapsychology: for example, the relation between energy and structure, and that between thought (meaning) content and function. Colby's treatment of both of these suggests interesting theoretical possibilities. Second, for the few who are conversant with metapsychology, there are many ideas, intuitive perceptions, and hints between the lines.

Considering that this volume has—as it were—no predecessors, it is a bold undertaking. It is to be hoped that it will be read, that it will stimulate specialists to work in metapsychology, and nonspecialists to begin to discover a different aspect of psychoanalysis from that to which they are accustomed.

Yet the volume's importance is matched by its inadequacies. It consists of two parts: one attempts to review Freud's metapsychology and the models it is built on, the other to suggest a different model replacing Freud's.

The weaknesses of the first part are rooted in its being scarcely more than a preparation for the second. The presentation of Freud's metapsychology is, to say the least, incomplete. For example, only two of his "Papers on metapsychology"—"On narcissism: an introduction" and "The unconscious"—are even mentioned. The work of other students of metapsychology fares no better: outstanding ones like Hartmann, Kris and Loewenstein merit only two references; Hartmann's major study, "Ich-Psychologie und Anpassungsproblem" ("Ego psychology and the problem of adaptation," is not referred to. Ill-informed passages and misunderstandings are embarrassingly frequent. Still the book gives the impression of serious intent handicapped by lack of tradition rather than by carelessness or malintent.

The principal aim of the book—to replace Freud's outdated and mechanical models with a modern and dynamic one—is not realized. While Freud's theory is mechanical in its trappings and dynamic in its core, Colby's is dynamic in its intent but becomes mechanical in its execution. Yet Colby does introduce the reader to Freud's reflex, tension-reduction, and id-ego-superego models as well as to his own cyclic-circular model. The topographic reflex model represents the course of excitation, in the psychic apparatus, from perceptual stimulation to motor action. The economic tension-reduction (pleasure principle) model represents the tendency of psychological processes to prevent and to reduce tension accumulation. The structural id-ego-superego model is familiar. Colby's own model is an attempt to replace these three models by a single one and to cope more adequately with the problem all these models are designed to solve: the integration of motivations and past experience with current environmental input. It is not possible to discuss here the many cogent points Colby makes in regard to the nature of this integration or to analyze the shortcomings of his treatment of Freud's models or the inadequacies of his own model. The book's main weakness can be revealed, however, by raising the questions: What can we gain by replacing the models of a theory which has not yet been systematized and whose limits of usefulness have not yet been explored? Can one, under these conditions, hope to demonstrate which model is more parsimonious or more powerful? What can be taken as an answer to these questions in Colby's book is singularly weak. And yet, even in this respect there is something to be said for his bold attempt: it might contribute toward weakening an orthodoxy which discourages attempts to take a new look at Freud's theories.

To the specialist, the book as a whole conveys two emphases. It stresses the need for unfettered theoretical speculation and the need to keep in harmony with the conceptions of present-day science (particularly physics). Both these emphases are justified.

But in regard to the first emphasis, Colby fails to show how the empirical data of psychoanalysis can impose discipline on free speculation. This lack will certainly limit the impetus the book can give to systematic theory-building in psychoanalysis, and it may well repel the nonspecialist, leading him to the conclusion that this general theory, just like the special one, lacks that ingredient of cohesion and discipline which makes theories amenable to empirical decision.

The second emphasis consists of frequent references to specific concepts of present-day physics, but no attempt to introduce them systematically to the specialist is made. The nonspecialist in turn may be taken aback, both by the frequency of these references, which may sound to him like lip service, and by the lack of exposition, which may make him wonder how well-digested these concepts

of physics are and how relevant the link (or how premature the jump) to psychological concepts is. As an introduction for the nonspecialist, the book flounders on an obstacle common to such an attempt in any science: it fails to make the relevance of the theory to observations plausible.

It would be regrettable if, in spite of these shortcomings, this book were not read. What it deals with is at least a possibly—and to my mind, probably—crucial frontier of *psychology's* development into a unified science. Clinical psychoanalysis is in many ways a self-contained specialty, but psychoanalysis at large *is* psychology. It is a psychology built to account for vital phenomena of human behavior, not tackled by those theories which arose from experiments. Metapsychology holds the promise that it can bring this psychology to a level of theoretical generality where its unification with experimentally derived theories, or at least its experimental verification, will be possible [see *Theoretical Models and Personality Theory*, D. Krech and G. S. Klein, Eds., and *Systematic Resources of Present-Day Psychology*, S. Koch, Ed.]. Though this promise may prove to be an illusion, still it must be given a try. Colby's book is a contribution toward making such a try possible. Its shortcomings cannot be overlooked, but they can be accepted as reflections of the present state of psychoanalytic metapsychology and of psychology at large.

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Recent Advances in Science. Physics and applied mathematics. Morris H. Shamos and George M. Murphy. New York University Press; Interscience, New York, 1956. 384 pp. Illus. $7.50.

This volume includes papers that were presented at a symposium on recent advances in science, held at New York University in the spring of 1954 for representatives of industrial, government, and university laboratories. Although the volume did not appear until nearly 3 years after the symposium, it represents an important addition to the library of review articles in major fields of physics. The contents and distinction of the book are probably best shown by a simple listing of the chapters and their respective authors: "Methods of applied mathematics," Richard Courant; "The future of operations research," Philip M. Morse; "Atomic structure," I. I. Rabi; "Microwave spectroscopy," C. H. Townes; "Nuclear structure and transmutation," H. A. Bethe; "Elementary particles," V. F. Weisskopf; "Electronuclear machines," Leland J. Haworth; "Neutron physics," Norman F. Ramsay; "Transistor physics," William Shockley; "Ferromagnetism," R. M. Bozorth; "Cryogenics; very low temperature physics and engineering," F. G. Brickwedde; and "Physics and the engineer," Edward U. Condon.

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Handbuch der Physik. vol. VII, *Crystal Physics 1*. S. Flügge, Ed. Springer, Berlin, 1955. vii + 687 pp. Illus. DM. 122.50.

Crystal Physics 1 consists of four long articles: "Crystallography," by Heinz Jagodzinski, of Würzburg (103 pages); "Lattice theory of the mechanical and thermal properties of crystals," by Günther Leibfried, of Göttingen (221 pages); "The specific heat of solids," by M. Blackman, of London (58 pages); and "Theory of crystal imperfection," by Alfred Seeger, of Stuttgart (282 pages). These are followed, as is usual in the *Handbuch der Physik*, by subject indexes in German and English. Blackman's article is in English, the other three are in German.

The first article develops the subject of possible crystal lattices from the standpoint of symmetry operations. Tables compare the notations of different authors. Next, the geometric character of the different properties is treated, then the external geometry of crystals. Finally, the connection between chemical formula and crystal structure is discussed from a qualitative standpoint.

Leibfried's article is, so to speak, a new, more profound edition of Born's pioneer work. Although it has not been possible for him to present all the details, Leibfried always gives the fundamental quantum-mechanical equations, which consider the crystal as made up of nuclei and electrons, and indicates how one gets from that point to the coarser treatment which considers whole atoms or ions as the building stones. The different types of energy interactions are described, and the successes and the difficulties that are encountered in explaining why a particular substance has a particular lattice are indicated. Next, the lattice theory of deformation and stresses is given and compared with the continuum expressions. A very useful feature here is the tabulation of constants for simple lattice types (that is, expressions of elastic constants through intermolecular spring constants). The equations of motion from which the lattice vibrations are calculated are a consequence of the preceding theory. Then follows the discussion of the more subtle case of ionic crystals and the coupling between lattice wave and electromagnetic waves, but crystal optics is not treated in detail. The thermodynamic properties are next taken up, and here there is some duplication with the next article. There follows an interesting discussion of the non-Hooke's law terms, which are responsible for heat expansion and thermal conductivity. The lack of a complete theory is emphasized.

Blackman has specialized for many years in calculating the distribution function of lattice vibrations, which governs —although not very sensitively—the specific heat. He develops here the methods which have become recently available but emphasizes that each case demands a separate calculation. In the simplest approximation one uses a Debye function, but, to get agreement with lattice theory and experiment, one must allow the "constant" Debye temperature to vary with temperature. In polyatomic crystals, Blackman always uses, in this approximation, pure Debye functions, not, as is often done, sums of Debye and Einstein functions. Detailed comparison with the experiment are made.

The subject of crystal defects has been developed only in recent years; there exist only a few coherent presentations that are as detailed and extensive as that of Seeger. Crystal defects are divided according to their dimensions into those of zero dimensions—empty lattice places, dislocated atoms—and those of one or two dimensions (dislocations, grain boundaries). The former may be a result of thermal equilibrium, and a detailed treatment is given of their number, heat of formation, and migration (diffusion). Those of the second kind are responsible for the diminished mechanical strength of crystals. They may be line dislocations, which wander under the influence of stresses and produce slip, or screw dislocations, which are important in crystal growth and are, in fact, decisive for the growth of ionic crystals.

In the whole volume, the printing is excellent and there is an abundance of illustrations. These are particularly valuable because so many geometric questions are discussed; in addition, many experimental results are presented graphically, especially in Blackman's article. The proofreading must have been exceptionally careful; I cannot remember having noticed any printing errors.

In one point, at least, some of the articles differ from those in the first two editions of the *Handbuch*. The latter tried to give a complete bibliography of their subject, so that it was sufficient for a research worker to take the *Handbuch* as a starting point and search the literature for only about a year prior to the publication date. Obviously, as a matter of policy, the present encyclopedia treats this problem differently. This is illustrated in the present volume.

The articles are, in general, excellent representations of the present state of knowledge, but if one is interested in a particular disputed point or in whether someone else in the past has expressed a particular idea, one cannot rely on the fact that the dispute or the idea is not cited in the *Handbuch*. I assume that the present policy is necessary because of the enormous mass of material to be covered, but I cannot avoid being sorry that this is so.

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New Books

Man into Space. New projects for rocket and space travel. Hermann Oberth. Translated from the German by G. P. H. de Freville. Harper, New York, 1957. 246 pp. $4.50.

The Art of Painting. Leonardo da Vinci. Translated from the Italian by John Francis Rigaud, with an introduction by Alfred Werner. Philosophical Library, New York, 1957. 224 pp. $4.75.

Lascaux and Carnac. Glyn Daniel. Macmillan, New York; Butterworths, London, ed. 2, 1957. 127 pp. $3.

Genetic Mechanisms: Structure and Function. vol. XXI of *Cold Spring Harbor Symposia on Quantitative Biology.* Biological Laboratory, Cold Spring Harbor, New York, 1956. 410 pp. $8.

Trade and Market in the Early Empires. Economies in history and theory. Karl Polanyi, Conrad M. Arensberg, Harry W. Pearson, Eds. Free Press, Glencoe, Ill., 1957. 400 pp. $6.

Progress in Low Temperature Physics. vol. II. C. J. Gorter, Ed. North-Holland, Amsterdam; Interscience, New York, 1957. 491 pp. $10.75.

Geometric Integration Theory. Hassler Whitney. Princeton University Press, Princeton, N.J.; Oxford University Press, London, 1957. 401 pp. $8.50.

Practical Physics. A course of introductory experiments. R. W. Parsons. Hong Kong University Press, Hong Kong; Oxford University Press, London, 1957. 89 pp.

Soil Conservation. J. H. Stallings. Prentice-Hall, Englewood Cliffs, N.J., 1957. 586 pp. $8.50.

Man as an Animal. W. C. Osman Hill. Hutchinson, London, 1957. 176 pp. $1.50.

Psychological Aspects of Aging. Proceedings of a conference on planning research, Baltimore, Md., 24–27 Apr. 1955. John E. Anderson, Ed. American Psychological Association, Washington, D.C., 1956. 331 pp.

Microbial Ecology. Seventh symposium of the Society for General Microbiology held at the Royal Institution, London, Apr. 1957. Cambridge University Press, Cambridge, England, 1957. 396 pp. $6.50.

Extinct Languages. Johannes Friedrich. Philosophical Library, New York, 1957. 192 pp. $5.

Solid Geometry. Hugo Mandelbaum and Samuel Conte. Ronald, New York, 1957. 261 pp. $4.

Man among the Stars. Wolfgang D. Müller. Criterion Books, New York, 1957. Translated from *Du Wirst Die Erde Sehn als Stern,* Deutsche Verlags-Anstalt. 307 pp. $4.95.

The Handbook of Private Schools. An annual descriptive survey of independent education. 1957. Porter Sargent, Boston, ed. 38, 1957. 1120 pp.

Carotene. Its determination in biological materials. V. H. Booth. Published under the auspices of the Society for Analytical Chemistry. Heffer, Cambridge, England, 1957. 126 pp. 18s.

Radio Aids to Air Navigation. J. H. H. Grover. Philosophical Library, New York, 1957. 148 pp. $6.

A Guide to the Literature of Chemistry. E. J. Crane, Austin M. Patterson, and Eleanor B. Marr. Wiley, New York; Chapman & Hall, London, ed. 2, 1957. 412 pp. $9.50.

Report of the Meeting on Semiconductors Held by the Physical Society in Collaboration with British Thomson-Houston Ltd. Rugby, Apr. 1956. Physical Society (London), London, England, 1957. 153 pp. Members, 12s. 6d; nonmembers, 20s.

Teaching Science in the Secondary School. R. Will Burnett. Rinehart, New York, 1957. 394 pp. $5.25.

Methods of Biochemical Analysis, vol. IV. David Glick, Ed. Interscience, New York, 1957. 371 pp. $8.50.

Gas Chromatography. A. I. M. Keulemans. C. G. Verver, Ed. Reinhold, New York; Chapman & Hall, London, 1957. 236 pp. $7.50.

Traité de Microscopie. Instruments and techniques. A. Policard, M. Bessis, and M. Locquin. Masson, Paris, 1957. 614 pp. F. 5200.

Annual Review of Medicine, vol. 8. David A. Rytand and William Creger. Annual Reviews, Palo Alto, Calif, 1957. 537 pp. $7.

The Microbial World. Roger Y. Stanier, Michael Doudorff, and Edward A. Adelberg. Prentice-Hall, Englewood Cliffs, N.J., 1957. 704 pp. $8.

Dairy Microbiology. Edwin M. Foster, F. Eugene Nelson, Marvin L. Speck, Raymond N. Doetsch, and Joseph C. Olson, Jr. Prentice-Hall, Englewood Cliffs, N.J., 1957. 492 pp. $10.

Development of Vertebrates. Emil Witschi. Saunders, Philadelphia, 1956. 604 pp. $8.50.

Readings in Marriage Counseling. Clark E. Vincent. Crowell, New York, 1957. 12 pp. $4.50.

Thought, Life and Time as Reflected in Science and Poetry. H. G. Wood. The tenth Arthur Stanley Eddington memorial lecture. Cambridge University Press, Cambridge, England, 1957 (order from Cambridge Univ. Press, 32 E. 57 St., New York). 64 pp. Paper, $0.90.

Plant Protection Conference 1956. Proceedings of the second international conference at Fernhurst Research Station, England. Edited by Plant Protection, Ltd. Academic Press, New York; Butterworths, London, 1957. 326 pp. $9.

A Text-Book of Surgical Pathology. Charles F. W. Illingworth and Bruce M. Dick. Little, Brown, Boston, ed. 7, 1956. 738 pp. $14.

Miscellaneous Publications

(Inquiries concerning these publications should be addressed, not to Science, *but to the publisher or agency sponsoring the publication.)*

Teaching about Cancer. A guide to source materials and information prepared to help secondary-school administrators and teachers in developing instruction on cancer suitable to their curriculum requirements. American Cancer Society, New York, 1957. 48 pp. Free on request.

Institute of International Education 37th Annual Report, 1956. Institute of International Education, New York, 1957. 56 pp.

Interim Report to the Congress from the Commission on Increased Industrial Use of Agricultural Products. J. Leroy Welsh, Karl D. Butler, George H. Coppers, Charles R. Sayre, Frank J. Welch. c/o U.S. Department of Agriculture, Washington, D.C., 1957. 190 pp.

Annotated Tables of Strength and Elastic Properties of Rocks. Paper No. 663–G. Rudolph G. Wuerker. Petroleum Branch, American Institute of Mining Engineers, Dallas, Tex., 1956. 22 pp. Single copy free to AIME members; $0.25 per additional copy.

Directory of Fisheries Institutions: Asia and the Far East. United Nations Indo-Pacific Fisheries Council secretariat, Ed. Food and Agriculture Organization of the United Nations, Regional Office for Asia and the Far East, Bangkok, Thailand, 1957. 78 pp.

American Cooperation with Higher Education Abroad. A survey of current programs. Bull. 1957, No. 8. Paul S. Bodenman, with the cooperation of the Inter-Agency Committee and the President's Baylor Proposals. 220 pp. $0.75. *Opening Enrollment in Higher Educational Institutions: Fall 1956.* Circ. No. 496. M. Clemens Johnson and C. George Lind. 46 pp. $0.35. *Trends in Significant Facts on School Finance, 1929–30 to 1953–54.* Circ. No. 498. Clayton D. Hutchins, Albert R. Munse, Edna D. Booher. 84 pp. $0.60. U.S. Department of Health, Education, and Welfare (order from Government Printing Office, Washington 25, D.C.), 1957.

Early White Influence upon Plains Indian Painting. George Catlin and Carl Bodmer among the Mandan, 1832–34. Misc. col., vol. 134, No. 7. Publ. 4292. John C. Ewers. 11 pp. *A Skull of the Bridger Middle Eocene Creodont, Patriofelis Ulta Leidy.* Misc. col., vol. 134, No. 8. Publ. 4293. C. Lewis Gazin. 20 pp. Smithsonian Institution, Washington, D.C., 1957.

Production and Mill Utilization of Feed Grains in Arkansas. Bull. 583. W. R. Morrison. 30 pp. *When to Harvest Oats for Hay and Silage.* Bull. 586. R. L. Thurman, O. T. Stallcup, J. L. Stephens, N. E. Justus. 18 pp. *Arkansas Soybean Variety Trials, 1951 to 1956.* Rept. ser. 65. C. E. Caviness and P. E. Smith. 11 pp. Agricultural Experiment Station, College of Agriculture and Home Economics, University of Arkansas, Fayetteville, 1957.

The Scalp and Its Care. With clinical notes on dandruff and seborrhea. Schering Corp., Bloomfield, N.J., 1957. 25 pp.

Meetings and Societies

Elementary Particles, Atomic Power, and Drift of Continents

Last year once more 22 Nobel prize winners from eight different countries were brought together in the last week of June for their yearly meeting by their common bonds, the Nobel prize and natural science. Aside from the stream of congresses in a quiet corner on the Bodensee, Lindau became through physics, for a few days, a republic of scientists.

Today we know that atoms consist of numerous elementary particles. Especially in the past few years we have learned many new things about these particles. Werner Heisenberg (Göttingen) discussed in his lecture—which may well have been the most important of this year's meeting—his position on the problems in the theory of elementary particles. Today we know approximately 25 such particles which are very similar to the building stones of matter, some of which decay, however, in a fraction of a second. At the end of the 1920's theoretical physics attempted to describe these particles mathematically by applying quantum theory to wave theory. Actually, however, no basic results were obtained with these methods. There exists a conflict between quantum mechanics (uncertainty relation) and the space-time structure of the special relativity theory, according to which all effects are propagated only with the velocity of light. Using the approximation theory by altering the basis of the quantum and the relativity theory, and through recalculations by Bethe that resulted in a correction of the previous theory by Sommerfeld and Dirac, calculations that agreed well with experimental measurements were performed. However, it seems impossible with these operations to unite the 25 elementary particles into a common mathematical system of formulas.

The Göttingen investigations by Heisenberg deal with a new mathematical equation that attempts to embrace all elementary particles and to reduce them to a common denominator. The resulting basic equation is supposed to play the part of a model which represents a system of elementary particles and which is simpler than the real one occurring in nature. By applying the new system of formulas, new perceptions result which agree with experimental results. This model of elementary particles is surely too simple. The new system of mathematical equations advocated by Heisenberg lacks a degree of freedom that still has to be built into it in the near future. One will be able then, according to Heisenberg, to explain nearly all conservation theories of elementary particles and in this way find a formula for the experimental results.

The lecture of Hideki Yukawa (Kyoto, Japan) also dealt with elementary particles. He was able in 1953 to report in Lindau about his research toward creating a common theory for elementary particles. Yukawa now has to depart in many points from his former conceptions.

P. A. M. Dirac (Cambridge, England) dealt in his lecture with one particle only, namely, the electron, for which there is yet no complete theory available. According to the classical picture, the electric field around an electron at rest is *circularly symmetrical* close to the electron. According to the new conception, the electric field is totally concentrated in a single "Faraday" line of force emanating from the electron. Therefore we might have to say good-by to the circular symmetry, so Dirac thought.

"We shall now embark into a great scientific and technologic adventure to tame nuclear energy in order to make a new source of power accessible to the world in addition to energy sources from fossil fuels. For this purpose we shall use the heat developed in splitting uranium in nuclear reactors in order to produce steam for operating the turbines of alternating-current generators of power plants." With these words the English atomic physicist, John Cockcroft (Harwell, England) started his lecture that entered into the scientific and technical problems of utilization of atomic energy. Today we know many types of nuclear reactors, and more will be added in the future. However, up to now two types have mainly been developed, the first type in England and France, the other mainly in the United States and the U.S.S.R.

The English reactors use as fuel mainly natural uranium and a graphite moderator with gas as heat exchanger. The reaction of nuclear fission in the first reactor in the British Calder Hall station started some time ago, when for the first time uranium rods were introduced into the machine. One assumes that the two reactors are going to be in full production at the beginning of 1957 and that the station is going to deliver 70,000 kilowatts to the electric supply net.

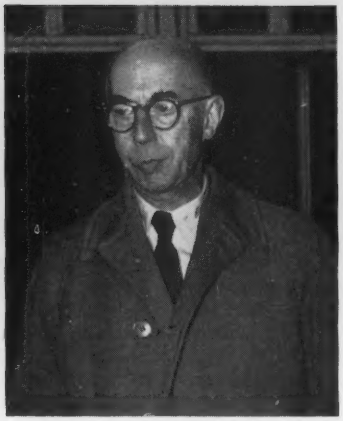
The first industrial nuclear energy stations to be built for the electric power authorities, in which two reactors each produce heat, are in the planning stage. They are supposed to have a considerably larger capacity than Calder Hall. In this kind of reactor—a heat source of 2000 to 3000 kilowatts per ton of uranium—the fuel elements may remain from 1000 to 1500 days before the central uranium rods have to be replaced. In applying a systematic, repeating sequence, it is possible to produce for each ton of uranium an amount of energy equal to 30,000 tons of coal, and in this way the raw material costs of these reactors can be kept down.

The second type of nuclear energy station utilizes ordinary water as moderator and as heat exchanger. Despite the inherent difficulties connected with this type of station, enough heat can be produced to develop up to 180,000 kilowatts of electric power. The use of water results, unfortunately, in difficult corrosion problems in addition to the task of planning the machinery.

Two other reactors may become com-

Left to right: P. A. M. Dirac, H. Yukawa, and W. Heisenberg.

John Cockcroft.



G. Hertz.

P. M. S. Blackett.

petitors of the water-cooled machines. One uses an organic liquid—for example, diphenyl—in place of water and thus reduces the corrosion problem. The other uses a graphite moderator and liquid sodium as heat exchanger.

Breeder reactors are another important group of reactors. The Harwell reactor, Zephyr, was built for the study of nuclear properties of breeder reactors of fast neutrons. In Dounreay, Scotland, a breeder reactor designed to develop 60,000 kilowatts is being built.

Another possible breeder reactor, the homogeneous water reactor, uses uranyl sulfate as liquid fuel in heavy water. It is a breeder reactor of slower neutrons. This reactor may have very low fuel costs; however, it has corrosion difficulties which have not yet been solved. In Great Britain it is the opinion that a gas-cooled reactor with graphite as moderator and natural uranium as fuel is completely suitable for solving the problem of new energy sources for the United Kingdom.

In this connection, the separation of isotopic mixtures plays an important part. The isotopes that accumulate in the reactors have to be separated as elegantly and profitably as possible. Gustav Hertz (Leipzig), a specialist in the field of isotope separation, described in his lecture the different separation methods which are applied according to the composition of the mixture. For example, the magnetic separation method is, with the exception of rare gases, basically suitable for all elements. The capital investment in this method is, however, very great, and to get only a few grams, several days of operation are necessary.

Contrary to the magnetic-separator method, which with a single application makes an almost complete separation of the isotopes possible, the method using the thermal motion of the molecules produces a small result with only a single stage. One distinguishes here two groups: (i) in the first group, a procedure is involved in which a stream of the gas mixture to be separated is split up into two parts of different composition; (ii) in the second group, a stationary condition is involved in which a different isotopic composition exists at different points, separated by space.

As an example of the first group, a separation by diffusion through a porous wall was shown as well as the so-called "separation jet" in which the outer layer of a gas stream flowing into a vacuum is peeled off. Examples of the second group are separations in the gravitational field which are applied in the centrifuge, thermodiffusion, as well as the method of diffusion against a vapor stream. The latter arrangement is used for the construction of a separation pump which at the same time separates an isotope mixture and provides the necessary circulation in a multiplicator circuit.

Very useful in the procedure of the first group is a diffusion circuit, a commonly used series connection in which each separation link passes its light or heavy fraction to its neighbor. In the procedures of the second group, the principle of countercurrents in a separation tube, which was first developed by Clusius, is used. It can be shown that the same rules are valid for both arrangements so that the countercurrent columns can be treated in the same way as the diffusion circuits.

It has been known for years that a volcanic rock—for example, lava—becomes magnetic when cooled below its Curie point. This magnetism receives a direction parallel to the direction of the surrounding fields and an intensity proportional to the field. This thermomagnetic remanence provides a method for following the direction and magnitude of the earth's magnetic field through geologic history. Many sediment minerals

Left to right: H. Yukawa, R. Kuhn (behind him G. Hertz, Fritz Zernike), Max Born, A. Butenandt (behind him Th. Reichstein), O. Hahn, W. Pauli, C. V. Raman (behind him G. Hevesy), W. Heisenberg.

are found magnetized in nature too, but they are much more weakly magnetized than are volcanic minerals. In recent years instruments that permit measurements of this magnetism have been developed.

The results which P. M. S. Blackett (London) obtained from magnetic changes of minerals were discussed in the last lecture of the meeting. On the basis of many measurements, Blackett arrived at the assumption that England has drifted toward the north in the last 150 million years, from a place much closer to the equator than it is today and that it turned clockwise more than 30 degrees. There exists a certain probability for the relative enlargement of the space between America and Europe, as is usually stated in the theory of Wegener of continental drift. Measurements on Indian stones prove without doubt that India was situated south of the equator 70 million years ago. Measurements in South Africa furthermore point to the fact that the African continent has drifted directly over the South pole in the last 300 million years. Considering these preliminary results, one can safely state that during the earth's history single land masses have traveled large distances relative to the poles. We do not yet know for certain whether the earth's crust as a whole has moved rigidly toward the poles or whether the large motions of the continents were only relative to each other. It is, however, nearly certain that a polar migration, as it is temporarily called, has taken place with probably remarkable drift value. There can be almost no doubt that in the next decade it will be possible to trace the major movements of the great continents during the earth's history in a fairly reliable manner in order to examine experimentally the old theory of Wegener.

The following lectures are mentioned briefly: Max V. Laue (Berlin) reported on, "From Copernicus to Einstein." The struggle of the world systems found an end only with Einstein, who was able in 1908–15 by his general relativity theory, rejecting Euclidean theory, to embrace the field of mechanical, electromechanical, and optical phenomena as well as the facts of gravitation. The text of this lecture will be published in full in *Naturwissenschaftliche Rundschau*. The advancements in physical optics were discussed by Fritz Zernike (Groningen, the Netherlands), who in 1932 introduced the phase-contrast procedure into microscopy through which a contrasting effect of uncolored objects through phase displacement of the light source is achieved. Max Born (Bad Pyrmont, Germany) in his contribution remarked on the foundations of the gas theory, and C. V. Raman (Bangalore, India) discussed the physics of crystals. He entered into the question of the new conceptions concerning the behavior and the properties of crystalline bodies as developed by himself and his coworkers on the basis of theoretical and experimental research.

The following Nobel prize winners were also present as discussion partners and listeners: K. Adler (Cologne), A. Butenandt (Tübingen-Munich), G. Domagk (Wuppertal), H. v. Euler-Chelpin (Stockholm), O. Hahn (Göttingen), G. Hevesy (Stockholm), R. Kuhn (Heidelberg), P. H. Mueller (Basel), W. Pauli (Zürich), Th. Reichstein (Basel), L. Ruzicka (Zürich), and F. Soddy (Brighton, Great Britain).

H. ROTTA

Stuttgart, Germany

We are indebted to H. Rotta, Stuttgart, editor of Naturwissenschaftliche Rundschau, *for permission to publish his report* [Naturw. Rundschau **9**, 441 (1956)] *and to Mrs. A. M. Akeley, department of physics, Purdue University, for the English translation.*

Development and Growth

The 16th annual symposium of the Society for the Study of Development and Growth will be held at the University of Rhode Island, Kingston, 19–21 June. The symposium topic will be "Developmental cytology, changes in nuclear and cytoplasmic constituents during development and differentiation." The speakers will include J. R. Preer (Pennsylvania), C. Partanen (Harvard), T. C. Hsu (Texas), G. Klein (Stockholm), W. Beermann (Marburg), H. Stich (National Cancer Institute of Canada), D. v. Wettstein (Stockholm), D. Fawcett (Cornell Medical School), A. Lehninger (Johns Hopkins), and S. Spiegelman (Illinois). The annual business meeting of the society and a smoker will be held on the evening of 20 June.

Saline Water Conversion

An International Symposium on Saline Water Conversion is now planned for the first part of November 1957 under sponsorship of the Office of Saline Water of the U.S. Department of the Interior, and the National Academy of Sciences–National Research Council. The program for the meetings, which will be convened in Washington, D.C., has been developed by a committee of six scientists and engineers. It covers such topics as power distillation, electrodialysis, osmosis, solar distillation, freezing, and other scientific approaches to the problem of conversion of saline water for agriculture, municipal, and industrial uses. The objectives are to bring together, on an international scale, active workers in these fields, in the interest of reviewing and recording progress and stimulating new approaches to this important aspect of basic and applied science.

Approximately 30 invitational technical papers will be presented by participating scientists and engineers from the United States, the United Kingdom, Europe, Africa, and other areas of the world concerned with these problems. The scientific papers presented during the 3-day conference will be published by the NAS–NRC in its numbered series of scientific and technical monographs. Further details will be available by early summer. Inquiries should be addressed to the Division of Physical Sciences, National Academy of Sciences, 2101 Constitution Ave., NW, Washington 25, D.C.

Society Elections

■ Federation of American Scientists, Executive Committee: chairman, Paul M. Doty, professor of chemistry, Harvard University, Cambridge, Mass.; v. chairman, Hans A. Bethe, professor of physics, Cornell University, Ithaca, N.Y. (and wartime head of the Theoretical Physics Division at Los Alamos Scientific Lab); sec., Paul F. Zweifel, Manager, Theoretical Physics, Knolls Atomic Power Lab, Schenectady, N.Y.; treas., Christian B. Anfinsen, biochemist and Chief of the Laboratory of Cellular Physiology and Metabolism, National Heart Institute, Bethesda, Md.

■ Society for American Archaeology: pres., George I. Quimby, Chicago Natural History Museum; 1st v. pres., Alex D. Kreiger, Riverside Municipal Museum; 2nd v. pres., Kenneth E. Kidd, The Royal Ontario Museum; treas., James L. Swauger, Carnegie Museum; sec., David A. Baerreis, Dept. of Anthropology, University of Wisconsin, Madison. The representative to the AAAS Council is Dorothy C. Jensen.

■ Georgia Academy of Science: pres., William H. Jones, Emory University; v. pres., Stephen Gray, Agnes Scott College; pres.-elect, M. H. Goodwin, USPHS Communicable Disease Center; sec., Marion T. Clark, Emory University; treas., James G. Lester, Emory University. The representative to the AAAS council is William H. Jones.

Forthcoming Events

July

3–6. Current Problems in Crystal Physics, conf. IUPAP and NSF, Cambridge, Mass. (J. S. Slater, Massachusetts Inst. of Technology, Cambridge 39.)

8–10. Astrophysical Symp., 8th internl., Liége, Belgium. (P. Swings, Institut d'As-

trophysique, Université de Liége, Liége.)

8–10. Endocrine Aspect of Breast Cancer, Internatl. conf., Glasgow, Scotland. (A. P. M. Forrest, Dept. of Surgery, Western Infirmary, Glasgow, W.1.)

8–12. Inter-American Cong. of Philosophy, 5th, Washington, D.C. (R. M. Chisholm, Brown Univ., Providence, R.I.)

8–12. Poliomyelitis Conf., 4th internatl., Geneva, Switzerland. (Secretariat, 4th International Poliomyelitis Conference, Hotel du Rhone, Geneva.)

8–20. Legal Medicine and Law-Science Problems, 1st American cong., Chicago, Ill. (Law-Science Inst., c/o School of Law, Univ. of Texas, Austin 12.)

9–11. Biological Symp., 8th annual, Univ. of Michigan, Ann Arbor. (B. L. Baker, Dept. of Anatomy, Univ. of Michigan, Ann Arbor.)

9–13. European Molecular Spectroscopy Conf., Freiburg, Breisgau, Germany. (R. Mecke, Dept. of Physical Chemistry, Univ. of Freiburg, Freiburg.)

9–13. International Cong. for the Study of Social Insects, Paris, France. (G. Richard, International Union for the Study of Social Insects, Faculty of Sciences, University of Rennes, Rennes, France.)

10–12. Thermodynamic and Transport Properties of Fluids, conf., IUPAC, London, England. (Institution of Mechanical Engineers, 1, Birdcage Walk, Westminster, London, S.W. 1.)

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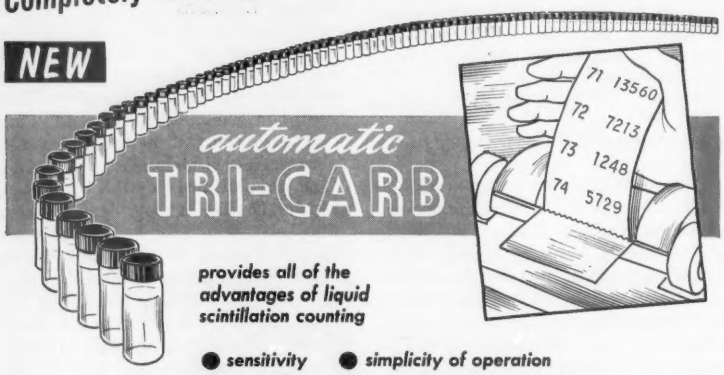

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10–17. International Union of Crystallography, 4th genl. assembly, Montreal, Canada. (G. A. Jeffrey, Chemistry Dept., Univ. of Pittsburgh, Pittsburgh 13, Pa.)

11–13. Applied Cytology, European Symp., Brussels, Belgium. (Secretary, Comm. on International Cong., American Cancer Soc., 521 W. 57 St., New York 19, N.Y.)

14–19. International Assoc. of Gerontology, Merano, Italy. (A. I. Lansing, Dept. of Anatomy, Univ. of Pittsburgh, Pittsburgh 13, Pa.)

14–20. Clinical Pathology, 4th internatl. cong., Brussels, Belgium. (M. Welsch, Service de Bacteriologie et de Parasitologie, Université de Liége, Blvd. de la Constitution, Liége, Belgium.)

15–18. Biochemistry of Lipids, International Colloquium, Oxford, England. (Dr. Sinclair, Laboratory of Human Nutrition, Oxford.)

15–19. Institute on College Administration, annual, Ann Arbor, Mich. (A. D. Henderson, 2442 U.E.S., Univ. of Michigan, Ann Arbor.)

16–19. American Malacological Union, annual, New Haven, Conn. (Miss M. C. Teskey, P.O. Box 238, Marinette, Wis.)

16–24. International Cong. for Pure and Applied Chemistry, 16th, Paris, France (R. Morf, Secy. Genl., IUPAC, Sandoz, S.A., Basel, Switzerland.)

20–21. Medical-Sociological Aspects of Senile Nervous Diseases, internatl. symp., Venice, Italy. (S. N. Feingold, Jewish Vocational Service of Greater Boston, 70 Franklin St., Boston 10, Mass.)

21–28. Neurological Sciences, 1st internatl. cong., Brussels, Belgium. (P. Bailey, National Institutes of Health, Bethesda 14, Md.)

23–24. Modern Electrochemical Methods of Analysis, Internatl. symp., Paris, France. (G. Charles, Ecole Superieure de Physique et de Chimie, 10, rue Vauquelin, Paris 5e.)

25–26. Structure Properties Relationships of Polymers (IUPAC), Paris, France. (International Union of Pure and Applied Chemistry, 4, Avenue de l'Observatoire, Paris 6e.)

25–29. Protein Chemistry Symp., IUPAC, Paris, France. (J. Roche, College de France, Place Marcellin Berthelot, Paris 5e.)

26–27. Experimental Psychology and Animal Behavior Section of International Union of Biology, Brussels, Belgium. (H. S. Langfeld, Dept. of Psychology, Princeton Univ., Princeton, N.J.)

26–27. Linguistic Soc. of America, Ann Arbor, Mich. (A. A. Hill, Box 7790, University Station, Austin 12, Tex.)

26–27. Military Psychology, internatl. symp., Brussels, Belgium. (National Academy of Sciences, 2101 Constitution Ave., NW, Washington 25.)

26–31. International Humanist and Ethical Union, 2nd cong., London, England. (American Humanist Assoc., Gate House, Yellow Springs, Ohio.)

26–1. International Congress on Nutrition, 4th, Paris, France. (Quatrième Congrès International de Nutrition, CNERNA, 71, boulevard Péreire, Paris 17e.)

(See issue of 17 May for comprehensive list)

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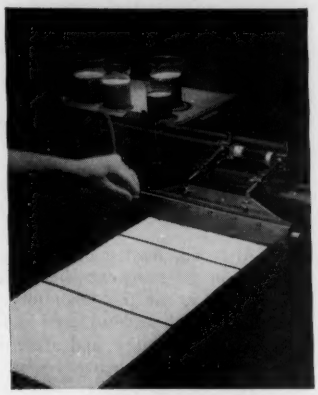

Here we are, seemingly hoist in the dark with our own photographic petard, while in the act of coating photographic emulsion on glass to keep the astronomers in business. Since the world's professional astronomers could all be comfortably accommodated in the stands of even a smallish town's ball park, the coating equipment we maintain for their benefit need not be very streamlined. It must, however, be very good, lest precious hours be wasted for magnificent instruments and men who have so much probing of the universe to cram into too brief lifetimes.

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LETTERS

The editors take no responsibility for the content of the letters published in this section. Anonymous letters will not be considered. Letters intended for publication should be typewritten double-spaced and submitted in duplicate. A letter writer should indicate clearly whether or not his letter is submitted for publication. For additional information, see Science **124,** *249 (1956) and* **125,** *16 (4 Jan. 1957).*

Passive Voice and Personal Pronouns

R. V. Ormes' judicious criticism of the passive voice [*Science* **125,** 529 (1957)] reminded me, by contrast, of my own too sweeping indictment of it a year ago. A young chemistry major took my remarks seriously and wrote a formal account of experimental procedure entirely in the active voice, using the first personal pronoun. The result was revealing. At least it convinced me that the passive voice is sometimes preferable to the active, and that criticism of it should be confined, like Ormes', to its abuse.

To illustrate, here is a passage on procedure, chosen at random from the *Journal of the American Chemical Society.* The original reads: "The thick oil was dissolved in ether, the solution was extracted twice with dilute alkali, and the combined basic extracts were washed with ether. The ether solutions were combined, dried and evaporated to give 2.8 g. of starting alcohol. The basic solution was acidified with dilute sulfuric acid and extracted with ether. The ether layer was washed with water. . . ."

Recast in the active voice, with the first personal pronoun, it reads: "We dissolved the thick oil in ether, extracted the solution twice with dilute alkali, and washed the combined basic extracts with ether. We combined the ether solutions, dried them, and evaporated them to give 2.8 g. of starting alcohol. We acidified the basic solution with dilute sulfuric acid and extracted it with ether. We washed the ether layer. . . ."

Except for the opening sentence, the original version is superior, primarily because it places the emphasis where emphasis logically belongs: on the process rather than on the agent. Coherence is better too: in the original, the substance named at the end of one sentence tends naturally to become the subject or subject modifier at the beginning of the next (". . . ether. The ether solution . . ."); in the revision, the reader is constantly brought back to "we" before he learns the next step in the on-going process.

But having stated the obverse or counterpart of Ormes' position with regard to the passive voice, I should like only to reinforce his position that the first personal pronoun is not an invariable sign of immodesty or subjectivity; sometimes considerations of objectivity and responsibility, no less than of style, demand its use. Certainly avoidance of it is no guarantee of virtue; I recall one immodest self-reference that went something like this: "Analysis of this problem is difficult, but after long deliberation, it was decided by this analyst to. . . ." Even worse is the pretense that beliefs are held and assumptions are made without danger of contamination from human fallibility. "It is assumed" may be quite all right for reminding a reader of assumptions customarily understood when certain equations are used, but the reader should know when the assumptions are original, and the simplest way to tell him is by saying "I have assumed. . . ."

After all, human agents are responsible for designing experiments, and they are present in the laboratory; writing awkward phrases to avoid admitting their responsibility and their presence is an odd way of being objective. P. W. Bridgman (*Reflections of a Physicist,* 1950, pp. 57–58) puts it even more strongly: "In suppressing these personal expressions I am doing an unnatural thing that sometimes demands obvious circumlocutions and always involves an element of convention and construction. If I want to express what obviously occurs, I have got to use the first person. Has it ever been adequately proved, or has ever the assumption been adequately examined that in forcing myself to speak non-personally I have not thrown away something vital?"

JANE J. ROBINSON
University of California, Los Angeles

University Responsibilities and Government Money

I agree very definitely with Paul Klopsteg [*Science* **124,** 919 (1956)] that the danger of government sponsorship of research is that of violation of the integrity of the universities in their research programs. However, the proposals and the suggestions made by Klopsteg are, in my opinion, diametrically opposite to those which would solve the problem.

In principle, Klopsteg proposes that whenever funds are granted to an institution for a particular project by a government agency, these funds should cover only part of the costs, and the remainder of the costs should be supported from the university's research funds, thus fulfilling the obligation of the university to support research. That this method of operation would lead toward the domination of the over-all research activity of an institution by granting agencies can be made clear by the following example.

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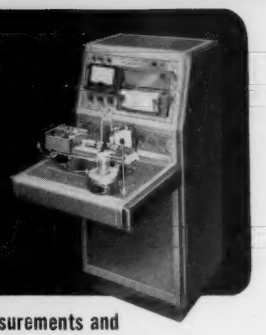

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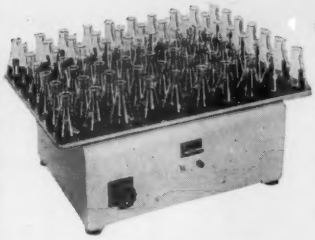

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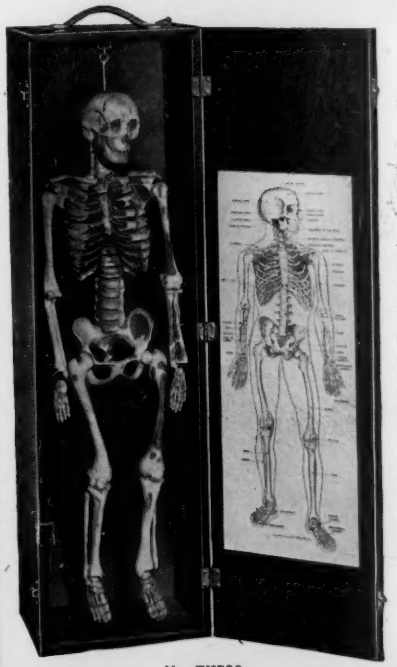

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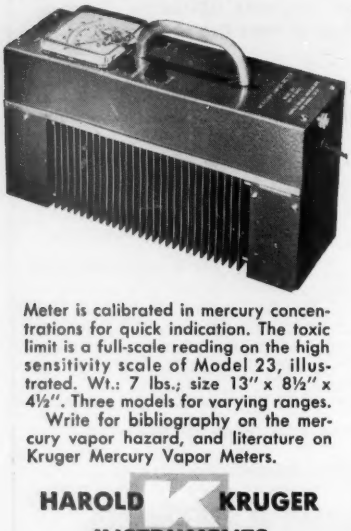

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6" x 9", 220 pp., 33 illus., references, index, cloth, May 1957.

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choose, using its best judgment for the benefit of mankind, which individuals and research programs it will support with this fund. We must further assume, which is generally true, that the institution would like to enlarge its research activities. This desire is certainly in line with the aims of Congress as specified in the formation of the National Science Foundation. To simplify our thinking, let us assume that the granting agency agrees to spend $5000 for 20 specific projects which it approves, provided that a corresponding and equal amount of money toward each of these projects is granted by the institution. Thus, the institution can double its research activity and spend $200,000 on research, provided that it undertakes projects approvable by the agency. On accepting the aid of the granting agency under this procedure, the institution becomes the servant of the granting organization, which effectively controls the whole research program at the university. Under the alternative system, the granting agency would support the total costs of ten specific projects at $10,000 each which are approved by the granting agency. At the same time, the institution will retain its integrity with respect to the expenditure of the $100,000 which it originally had, and it may now devote this money to any ten research projects which it feels, or its scholars feel, are best, regardless of the views of the granting agency. Thus the institution is no longer the complete slave of the granting agency.

Another insidious method of using the institution's funds in the support of research approvable by a granting agency is that of requiring that the principal investigator, who devotes a material part of his effort to the work supported by the grant, shall do so without charging his time to the grant, thus forcing the institution to carry his salary and its share of the overhead. In many cases, especially in the case of small grants, this cost is as large as, or larger than, the grant itself.

A further loss of control by the institution of the direction in which its own funds may be used through the procedure suggested by Klopsteg is brought about in a more subtle manner. Whenever a sponsoring agency fails to provide the full indirect costs of a project by limiting the allowance for them to 15 percent of direct costs or to some other arbitrary figure that is less than the true cost, the institution is forced to use a portion of its free funds to make up the difference. This must of necessity be true, since overhead rates are determined by distributing actual indirect costs over all programs, whether or not the overhead costs are provided by the granting agency. Since this indirect contribution to an added project through the failure to ob-

tain full overhead may be obscure, institutions are prone to accept the grant without qualm. However, when the number of projects reaches a significant size over several years, the total value of general funds used in this manner becomes an important drain on general funds that might otherwise be used for university-sponsored research, faculty salaries, or other activities traditionally associated with the institution. Klopsteg's implication that overhead funds are "uncommitted money" would appear to indicate his failure to understand the concept of indirect costs. Expenses for which overhead allowances are made must be paid by the institution. If the overhead allowances themselves are identified as "uncommitted money," then other available "uncommitted money" must be used to pay for the overhead expenses. There can be no net gain in "uncommitted money" from overhead allowances in the long run, for administrative costs must be paid, research buildings and equipment must be maintained and replaced, and the library facilities must be available for research workers. It is these costs that an overhead allowance is designed to cover. It does not increase the volume of free funds in an institution.

CARL C. CHAMBERS
University of Pennsylvania, Philadelphia

My purpose in publishing the article to which Carl Chambers refers, and the one in the next following issue of *Science*, has been accomplished when thoughtful, judicious persons like Chambers are moved to comment on the problems discussed. Whether our views coincide or differ matters little. What is important is recognition of the problems, and action to solve them.

It is quite impossible within the scope of a letter and a response to reconcile all the divergent views, nor does it seem possible at all, for we are dealing with opinions based on appraisal and judgment of facts and assumptions. What I shall attempt to do is to clarify where it appears that Chambers misunderstood what I tried to convey.

One such instance appears in his second paragraph in which he makes a condensed and, I regret, an erroneous paraphrase of what I "propose in principle." I do not propose that "whenever funds are granted to an institution . . . by a government agency, these funds should cover only part of the costs." On the contrary, in those research areas in which by far the greatest volume of government money flows to the institutions, I have stated that all costs, direct and indirect, should be *adequately* covered. These areas are comparatively new in the research pattern at universities, having come into being under OSRD during World War II. Most of the work is applied, not basic.

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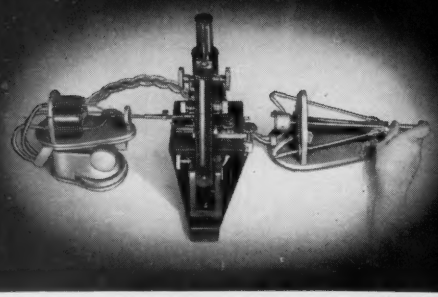

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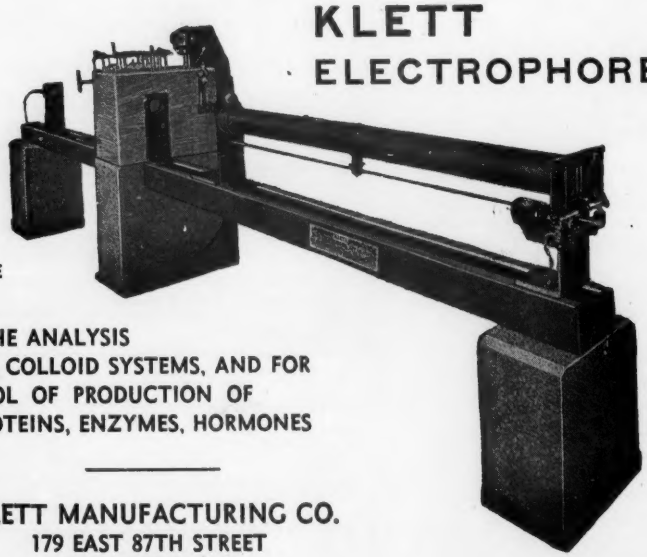

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The much smaller segment of research, aided by government, in which I strongly feel that institutions must maintain complete independence and integrity, is that which by tradition is the admitted responsibility of the university. To preserve the essential freedom, it is necessary that institutions receive financial aid from many sources, so that they may support competent scholars on their faculties in their intellectual pursuits, with complete absence of extraneous intervention, domination, or control. Money from private individuals and foundations assures such freedom. Money from government does not, since this is public money over which surveillance must be exercised in the public interest. If an institution, viewing a source of government funds as a virtually inexhaustible reservoir, insists that a grant or gift from such a source to help it in supporting scholarly research must cover fully every kind of outlay, direct and indirect, such insistence increases the danger of government control. This follows, because such discussions about overhead bring into the argument fiscal questions by participants who lack understanding of the ideals and functions of the university.

In dealing with private sources of gifts, the point is seldom made by universities that such sources must accompany their grants by an additional 25 to 50 percent of the principal amount tendered to cover indirect costs. Generally, private gifts are happily accepted as tendered, and great good will continues between the institution and the donor. If private sources could be stimulated to provide sufficient funds to enable universities and colleges to carry on their important functions, as is discussed in my second article, the question of overhead on gifts would fade away. To my knowledge, it never arose before government money came into the picture.

For a number of years, I have been in position to observe "from the inside" the increasing support of research through government funds. There is nothing insidious or sinister in the management of these funds by any agency. Those responsible for allocation and disbursement are honest, devoted public servants. Their duty to the taxpayer requires that they exercise judicious "control"; that is, they are responsible for seeing that funds under their supervision are handled properly under applicable statutes and the rules and regulations that have been derived from them. Because I feel so keenly the need for preserving freedom of action for the institutions, both intellectually and administratively, I feel growing apprehension over the fact that, as financial support from a given source increases, so also does the amount of control from that source increase.

If what I have written here and in my articles on these questions conveyed the impression that I fail to understand the concept of indirect costs, it is only because I failed to express myself clearly. During my many years as a business executive, I have had long, practical experience with that subject. Indeed, the problem of overhead is a perennial subject of discussion, if not controversy, among cost accountants. In its practical applications, it must in some of its aspects be handled arbitrarily. Probably it can never be settled to the satisfaction of everyone concerned with it. The use of the term *true cost* by Chambers implies a concept that is practically attainable. A method of determining the true cost of the contemplated basic research of a faculty scholar would be a major contribution to the art of accounting.

I respect Chambers and his views highly. I hope that it is not impertinent for me to say that the views are not unfamiliar to me, for I have heard them expressed in many discussions with university administrators. If he and I could discuss them in person, which I hope we may do, I am sure that we could substantially reduce our differences concerning the important questions under scrutiny here.

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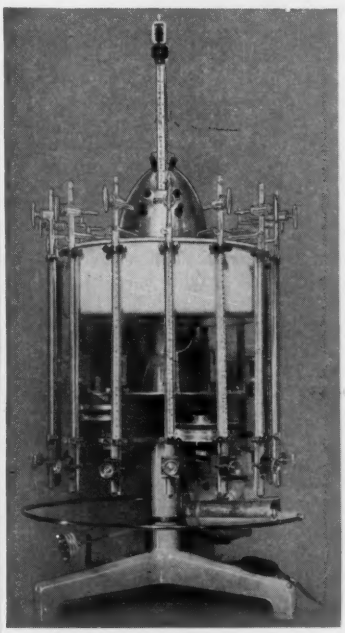

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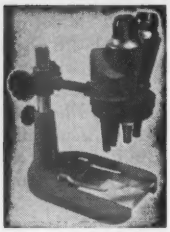

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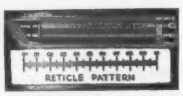

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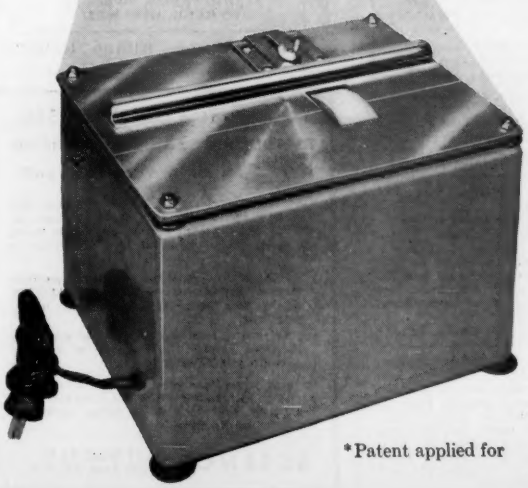

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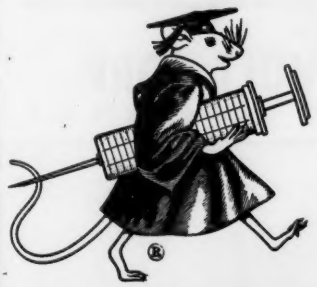

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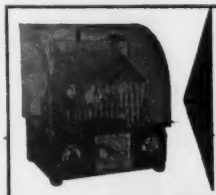

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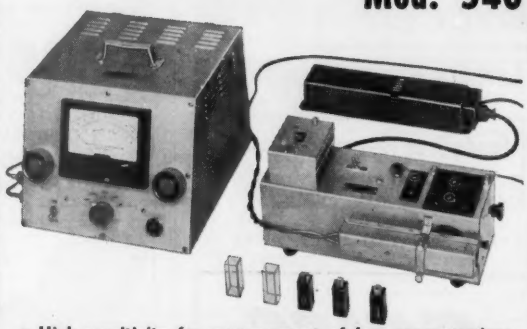

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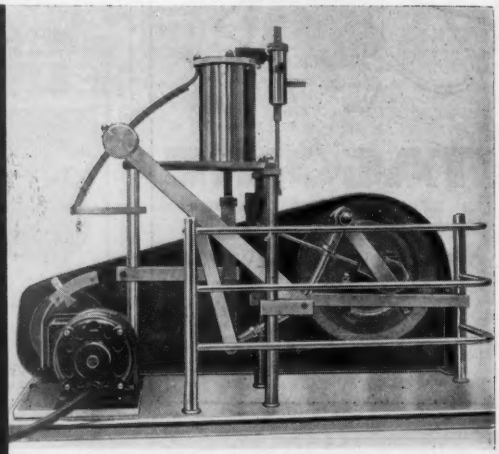

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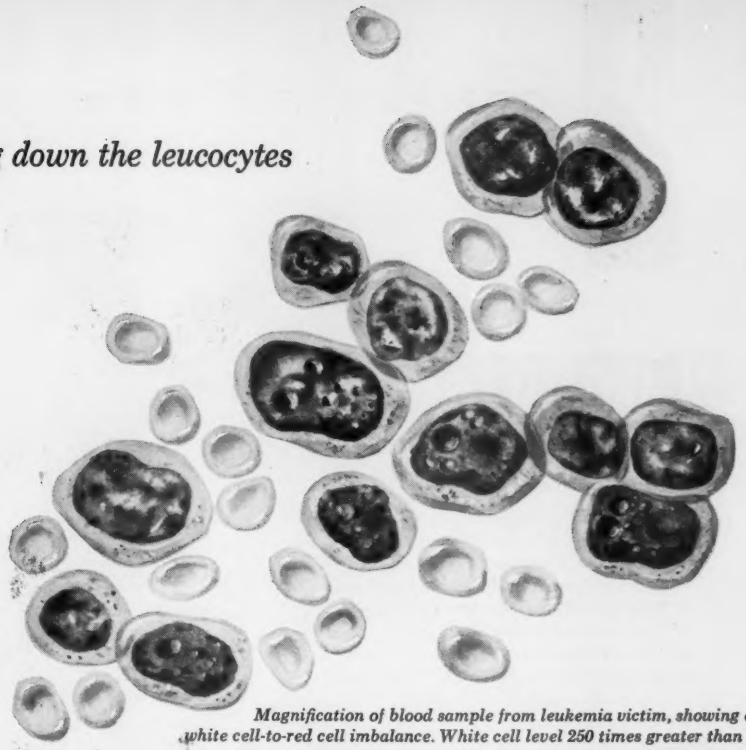

Magnification of blood sample from leukemia victim, showing extreme white cell-to-red cell imbalance. White cell level 250 times greater than normal.

Beckman® DK Automatic Recording Spectrophotometer speeds research in leukemia

Seeking to stop leukemia, medical scientists have learned how to slow it down. Inhibitors have been found that temporarily stop the abnormal production of *leucocytes*, white blood cells. But, because the body develops resistance to these present inhibitors, white cell metabolism must be better understood and more selective inhibitors discovered to permanently stop abnormal production of leucocytes.

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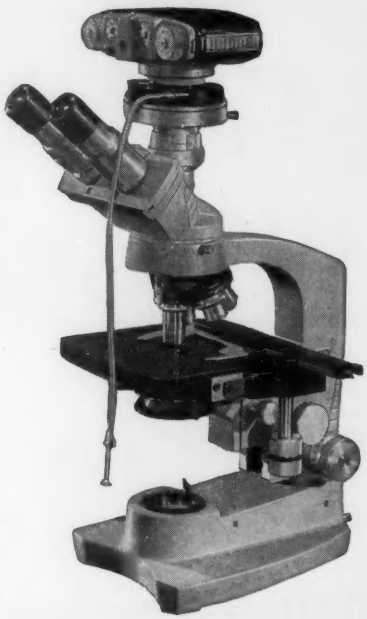

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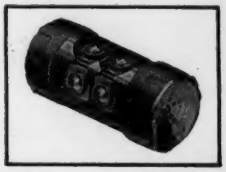

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